Consensus Statement

World Association of Veterinary Dermatology

Recommendations for approaches to methicillin-resistant staphylococcal infections of small animals: Diagnosis, therapeutic considerations, and preventative measures

Daniel O. Morris, DVM, MPH, DipACVD[1]; Anette Loeffler, DrMedVet, PhD, DVD, DipECVD, MRCVS[2]; Meghan F. Davis, DVM, MPH, PhD[3], Luca Guardabassi, DVM, PhD, DipECVPH[4]; J Scott Weese DVM, DVSc, DipACVIM [5]

1. Dept. of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA USA
2. Department of Clinical Sciences and Services, Royal Veterinary College, University of London UK
3. Depr. of Environmental Health Sciences, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD USA
4. Dept. of Biomedical Sciences, School of Veterinary Medicine, Ross University, Basseterre, St Kitts and Nevis West Indies
5. Dept. of Pathobiology, Ontario Veterinary College, University of Guelph, Guelph, ON Canada

Corresponding author: Daniel O. Morris, domorris@vet.upenn.edu

Consensus Statements

Staphylococcus pseudintermedius, *S. schleiferi* (including the coagulase-negative variant), and *S. aureus* are the primary pathogens encountered in small animal dermatologic practice. Clinical isolates of all three species commonly express methicillin resistance and multi-drug resistance.
In addition, several other species of coagulase-negative *Staphylococcus* (CoNS) have been reported to cause skin and soft tissue infections, and the pathogenic role of a CoNS must be deduced by the clinician on a case-by-case basis.
The pathogenic potential of any CoNS isolate obtained from a secondary skin lesion or a contaminated body site should be interpreted in light of the clinical disease process (urgency, co-morbidities, risk for adverse reactions to specific antibacterial drugs) and with respect to any other pathogenic species of bacteria that may be co-isolated with it.
Minimum reporting by microbiology laboratories should include complete speciation of staphylococci – regardless of tube coagulase status – and a complete antibiogram.
Topical therapy, using antibacterial agents and biocides with proven anti-staphylococcal efficacy, is the recommended treatment modality for any surface or superficial pyoderma involving MRS; particularly those with localized lesions, and for otitis and superficial wound infections.
Topical therapy should be used as the sole on-animal antibacterial treatment for surface and superficial infections whenever the pet and owner can be expected to be compliant.
Geographical differences exist in the availability and licensure of antimicrobial drugs for use in animals. Judicious use decisions need to take into account regional prescribing recommendations in veterinary and human medicine.
Empirical drug selection for systemic therapy is always contraindicated when a methicillin-resistant *Staphylococcus* (MRS) infection is suspected based on historical factors, due to the high prevalence of multiple drug resistance within these strains..
A restriction-of-use policy is recommended for use of glycopeptides (vancomycin, teicoplanin, telavancin), linezolid (oxazolidinon), anti-MRSA cephalosporins and potentially new compounds that may be approved in the future for treatment of multi-drug resistant pathogens of people.
There is little evidence for a difference in outcome between MRS and methicillin-susceptible *Staphylococcus* infections in animals, and that the prognosis for MRS skin infections in pets is good, depending on the underlying cause and co-morbidities.
There is currently not enough evidence to recommend routine decolonization of MRS carrier animals.
Molecular strain typing methods are research tools used to investigate the epidemiology and ecology of MRS. However, the clinical value of strain typing largely depends on the organism's population structure, the typing method(s) used, and the goals of the investigation. Strain typing often has no impact on patient- or clinic-level management, even in the context of most outbreaks.
In contemporary veterinary practices, routine cleaning and disinfection protocols are the cornerstone of hospital infection control. MRS are susceptible to commonly used disinfectants. Protocols should be designed to reduce or eliminate pathogenic burdens in the environment and on equipment. These protocols must be communicated clearly (and often) to the hospital team and practiced correctly and consistently.
Hand hygiene (proper washing/drying and use of alcohol-based hand sanitizers) is the main-stay of personal responsibility for infection control. No data exist regarding optimal personal protective equipment (PPE) practices for handling animals infected with MRS. However, the use of some degree of enhanced precautions to reduce contamination of clothing and skin is reasonable. Typically, this would consist of a gown or dedicated laboratory coat, and gloves.
Transmission of MRS by infected pets to other individuals in the home or community is known to occur, but data to guide recommendations are incomplete. In lieu of such data, it is reasonable to restrict animals from contact situations until treatment has started and a clinical response is evident. In the home, this could include social distancing from 'at risk' individuals and enhanced hygienic measures for the occupants and the environment.
Screening of clinically normal animals for carriage of MRS – regardless of the setting – rarely leads to clear and justifiable actions. Screening of humans leads to issues of confidentiality, and testing of clinic personnel (especially if not clearly voluntary and anonymous) could lead to a host of legal problems for clinic management. Testing of healthy individuals, particularly humans, should be a rare event that is based on a specific need and with a clear plan to act on the results.

Introduction:

Since the inception of antimicrobial drug use in the practice of modern medicine, staphylococci have evolved in response to the presence of antimicrobial drugs in biological systems. This evolution has included the *de novo* development or acquisition of antimicrobial drug resistance mechanisms, and the amplification and proliferation of epidemiologically successful strains of pathogenic staphylococci across human and animal populations. Currently, some degree of antimicrobial resistance has been documented within all *Staphylococcus* species that infect humans and domestic animals.[1,2] Pan-susceptible strains within any given species still exist, but have become uncommon in clinical practice.[3,4] Even staphylococci of low pathogenic potential (e.g. most coagulase-negative staphylococci) may harbor resistance determinants and serve as reservoirs for their transmission to species of greater pathogenic potential.[5] Collectively, the genus *Staphylococcus* is known to harbor resistance mechanisms to all antimicrobials that are available in clinical practice.[6-9]

In human medicine, methicillin resistance in *Staphylococcus aureus* has contributed to the medical and economic burdens associated with skin and soft tissue infections since the early 1960's.[10] In veterinary medicine, methicillin resistance has been recognized as a serious and widespread problem within the past decade, during which time its prevalence within populations of the *Staphylococcus* spp of greatest clinical importance to dogs and cats, namely *S. pseudintermedius, S. aureus* and *S. schleiferi,* has escalated rapidly.[3,4,11,12]

The term "skin and soft tissue infection" (SSTI) is used commonly in human medicine to describe an inflammatory response to microbial invasion of the epidermis, dermis, or subcutaneous tissues.[13] Although staphylococci are the most common cause of human SSTI, the term is not limited to staphylococcal infections. In dogs and cats, the terms superficial and deep pyoderma are used more commonly, and infection by a *Staphylococcus* spp is implied unless otherwise stated. Guidelines for the approach to treatment of SSTI of people were published in 2005[14] and updated in 2014.[15] The Infectious Diseases Society of America has also published guidelines for the treatment of human methicillin-resistant *S. aureus* (MRSA) infections, including SSTI, bacteremia and endocarditis, and infections of bone, joints, and the central nervous system.[16] While instructive to veterinarians, these guidelines do not address many of the nuances relevant to small animal veterinary practice. Guidelines for the treatment of canine pyoderma in general,[17] and for canine superficial bacterial folliculitis in particular,[18] have been published, but there are no comprehensive guidelines available regarding management of canine or feline SSTI caused by methicillin-resistant staphylococci (MRS). This document presents consensus statements regarding the laboratory diagnosis, transmission dynamics, and environmental mitigation of MRS, and provides management recommendations for cases of SSTI shown to be caused by them.

Methicillin resistance and multi-drug resistance:

Methicillin is a semi-synthetic, penicillinase-resistant penicillin that was developed to circumvent penicillin resistance mediated by staphylococcal penicillinases. Penicillinases are bacterial enzymes that deactivate both natural penicillins (penicillin G and V) and aminopenicillins (e.g. ampicillin and amoxicillin) by breaking the core structure of these β-lactam antibiotics. Shortly after the introduction of methicillin in human medicine, *S. aureus* developed resistance to it by acquisition of *mecA*, a gene encoding a specific penicillin-binding proteins (PBP2a) with low

affinity to all β-lactams, including cephalosporins.[20] Even if methicillin is no longer used in clinical practice, the term "methicillin-resistant" has persisted after the discovery of cephalosporins in the 1970s to indicate strains that are resistant to all beta-lactams except the newest generation of cephalosporins specifically developed for treatment of MRSA (e.g. ceftaroline). MRS may express co-resistance to any combination of other drug classes, including aminoglycosides, fluoroquinolones, lincosamides, macrolides, tetracyclines, potentiated sulfonamides, chloramphenicol, and rifampicin.[7] When a MRS strain expresses co-resistance to at least two additional antimicrobial classes, it may be referred to as multi-drug resistant (MDR), and the term extensively drug resistant (XDR) may be used if the strain is non-susceptible to all but two or fewer antimicrobial classes.[21] Both MDR and XDR strains have emerged worldwide amongst clinical MRS isolates from dogs and cats.[22]

Staphylococcal colonization:

Bacteria of the genus *Staphylococcus* are Gram-positive, facultatively anaerobic cocci that exist as part of the normal cutaneous and mucosal microbiota of mammals and birds. Most animals will be colonized by one or more *Staphylococcus* spp, with particular body sites being predisposed to colonization by certain staphylococcal species.[23,24] The origins of colonizing strains likely vary over a lifetime, but the first opportunity for acquisition occurs at the time of birth. It is known that puppies are colonized by maternal staphylococcal flora during the neonatal period,[25] and often maintain the strain transferred from the dam for many months after they are separated.[26] As adults, it may not be uncommon for dogs to harbor two or more genetically unrelated strains of *S. pseudintermedius* simultaneously but at different body sites.[27] The mouth appears to be the most consistent site for staphylococcal carriage in dogs and cats, followed by the perineum.[23] Co-carriage with multiple species of staphylococci at the same time, including pathogenic species, also is possible.[23, 28-30] Furthermore, a study of the complete microbiome present at putative staphylococcal carriage sites has suggested that feline nasal carriage of staphylococci is consistent with that carried by the humans in their households.[31]

Colonization implies that a bacterial population is self-sustaining for an extended period of time in the absence of disease. The term "carriage" is commonly used in a generic sense, when colonization has not been confirmed by longitudinal sampling of the animal. It may also be used to imply that a bacterial population is not biologically self-sustaining, but could be mechanically transmitted by its temporary host or from an environmental reservoir.[32,33] Human nasal carriage of *S. aureus* may be classified as "persistent" or intermittent" as defined by the nasal "culture rule", where persistence is reliably predicted by two positive nasal swabs collected at a one-week interval, from which a minimum number of colony-forming units is derived.[34] Such a rule has not been established for dogs or cats, and it appears that the nares might not be the most predictive site for sampling of dogs.[23,27]

In some cases, colonization by a particular staphylococcal species or strain may be short-lived, if a more dominant strain proliferates, out-competes, and displaces the original strain from its niche.[35] One example would be decimation of a colonizing staphylococcal population by an antimicrobial drug, and re-colonization by a strain that is resistant to that drug. It is widely believed that this is the mechanism by which MRS spread laterally across human and animal populations, and epidemiological evidence supports this assumption.[36,37]

Staphylococcal pathogenicity and virulence:

Several *Staphylococcus* species serve dual roles as commensals and opportunistic pathogens, and are capable of causing serious infections of the skin and many other tissues.[38-40] When cutaneous or systemic disease disrupts the skin's surface defense mechanisms, skin infection (bacterial pyoderma) or otitis externa may result. In the case of canine superficial bacterial folliculitis, infection is typically caused by the same strain of *Staphylococcus* that is present at carriage sites.[41] Invasive staphylococcal infections of deeper soft tissue planes, the genitourinary tract, respiratory tract, central nervous system, joints, bone, and body cavities may also result either from ascension along epithelial tracts, introduction via penetrating wounds, or through hematogenous spread.

The potential for pathogenicity is determined primarily by the arsenal of virulence factors expressed by any given *Staphylococcus* strain. An excellent review of staphylococcal virulence is provided by Rosenstein and Gotz[5]. Virulence factors may include expression of adhesins by which the bacterium binds to cells and extracellular matrix, formation of biofilm which protects the bacterium from the immune response, production of toxins (which may include cytolytic, exfoliative, enterotoxigenic, and superantigenic toxins), and expression of factors which assist in evasion of the host's immune response.[5,42] Of the latter, it is the ability to coagulate plasma *in vitro* —mediated by either a coagulase protein (produced by the *coa* gene) or a von Willebrand factor-binding protein— which is best known to clinicians as an indicator of pathogenic potential. Production of a coagulase factor promotes formation of a fibrin clot scaffold for tissue invasion, is associated with abscess formation, and protects staphylococcal microcolonies (*in vitro*) against neutrophils.[43,44] It should be noted that genetic expression of antimicrobial resistance is not a true virulence factor, i.e. a resistant strain is not necessarily more virulent than a susceptible one.

***Staphylococcus* species of relevance to veterinary medicine**

Coagulase-positive staphylococci (CoPS):

In veterinary medicine, it is the CoPS that cause the great majority of SSTIs. Historically, *S. intermedius* was the first CoPS recognized to be distinct from *S. aureus* in the mid-1970's. It was isolated from pigeons, dogs, mink and horses, and the species name derived from the investigator's observation that the biochemical characteristics of this new species were "intermediate" between those of *S. aureus* and *S. epidermidis*.[45] *S. intermedius* was subsequently identified as the major CoPS commensal and pathogen of dogs,[46] and many other domestic animal species. More recently however, the phylogenetic structure and nomenclature of *S. intermedius* has changed due to advances in molecular characterization.[47,48] The *S. intermedius* group (SIG) is now comprised of 3 genetically demonstrable species: *S. intermedius*, *S. pseudintermedius*, and *S. delphinii*, each of which occupy distinct ecological niches.[47] Of this group, the primary canine and feline pathogen is now known to be *S. pseudintermedius.*[49,50] This consensus document therefore uses the current nomenclature while recognizing that the older scientific literature (prior to 2007) references the primary canine and feline pathogen as *S. intermedius*.

The CoPS which may colonize the skin of the domestic dogs and cats have been well characterized, and include *S. pseudintermedius* and *S. aureus.*[23,27,29,30,51-53] *S. pseudintermedius* clearly dominates on dogs whereas in cats, studies differ on

whether *S. pseudintermedius* or *S. aureus* is carried most frequently.[29,54-57] It appears that the prevalence of *S. aureus* on canine and feline carriage sites is more common when these pets live with a person who has been recently diagnosed with MRSA infection.[23] *S. schleiferi, a* coagulase-variable species*,* has rarely been isolated from the healthy skin of either dogs or cats in cross-sectional studies of skin and mucous membrane carriage,[23,29,30] yet it is commonly isolated from skin and ear canal infections of dogs with histories of prior antimicrobial exposures.[39,58-60]

These three staphylococcal species cause the overwhelming majority of SSTI in dogs and cats,[3,4] and isolation of any one of them from a clinical sample should warrant careful consideration of the animal's need for antimicrobial therapy based on history and clinical signs. Anecdotally, another coagulase-variable species, *S. hyicus*, has occasionally been isolated from healthy cats[29] and from pyogenic infections of small animals,[61] although it is primarily known to veterinarians as the most common etiologic agent associated with porcine exudative epidermitis[1] ("greasy pig disease").

Coagulase-negative staphylococci (CoNS):

It is critical to note that *S. schleiferi* is a coagulase-variable species, currently classified as being comprised of two sub-species: *S. schleiferi* subsp *coagulans* (coagulase-positive) and *S. schleiferi* subsp *schleiferi* (coagulase-negative). However, recent genotypic and epidemiological studies have shown that these two subspecies are not genotypically distinct,[62.63] nor do they differ in their pathogenic effects.[39] This fact has led to a paradigm shift in the way veterinary microbiology laboratories must report culture and susceptibility results for CoNS (see below). The CoNS species *S. lugdenensis, S. haemolyticus, and S. epidermidis* have also been isolated from pyogenic infections of small animals, albeit rarely.[61,64]

Although CoNS have traditionally been considered to be non-pathogenic resident or transient commensals in animals, this viewpoint is likely oversimplified and in human medicine CoNS are known to be pathogenic in many settings.[65-69] This is in part due to the increasing prevalence of immunosuppression within the human population and use of invasive medical instruments, which have allowed greater susceptibility and exposure to less pathogenic organisms on a population-wide basis.[68] To compound the problem, CoNS commonly express MR and often even MDR,[70,71] and colonization with MR-CoNS is not uncommon in healthy and diseased individuals. However, with the exception of *S. saprophyticus* as a cause of urinary tract infections that arise outside of the healthcare setting, human infection by CoNS remains largely a hospital-associated problem in compromised hosts.[68]

In veterinary medicine, where most CoNS are still thought to be minimally pathogenic,[64] a common question posed by clinicians is what should be done when a lab reports that a CoNS has been isolated from a clinical sample. The consensus of this working group is that this interpretation should largely depend on how confident the clinician is that the "true" etiologic agent has been isolated. Coagulase-negative *S. schleiferi* should generally be considered pathogenic when isolated from inflamed tissue or a pyogenic fluid.[39,58,59] In the case of other CoNS species, the solution is much less clear. In general, if the culture sample was obtained from a "sterile" site using good aseptic technique (e.g., joint fluid, blood, CSF, closed body cavity, cystocentesis), or was collected from an intact primary skin lesion (pustule, bulla, non-draining abscess) and another more pathogenic bacterium was not also identified, the authors recommend that treatment may be considered and antimicrobials chosen (if needed) based upon susceptibility results. The microbiology laboratory may also be helpful to the clinician in making this assessment, based upon

the number of colony-forming units isolated from the sample. If the specimen was obtained from a contaminated site (such as the skin or ear canal surface, an open wound, the upper respiratory tract or oral cavity) the result should be interpreted with caution. In these cases, the clinician should consider repeating the culture, especially if extensive MDR presents a therapeutic dilemma and if the patient's health will not be compromised by waiting for additional test results. When a CoNS is isolated from a clinical sample as part of a mixed population of bacteria, consideration must be given to the composite antibiogram of these organisms and deference paid to any organisms known to have greater pathogenic potential. When conflicts of drug choice arise, antimicrobial therapy should be targeted toward the organism of greatest pathogenic potential.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Since the early 1960's, the prevalence of methicillin resistance in *S. aureus* has escalated in many countries and MRSA is a common cause of hospital-associated infections of people throughout the world.[72] During the mid-1990's, MRSA strains which cause SSTI in people with no known nosocomial risk factors arose *de novo* within the community.[72,73] These strains originally exhibited more favorable antimicrobial susceptibility profiles than hospital-associated strains, but express more virulence factors, such as the Panton-Valentine leucocidin toxin gene.[74,75] However, a progressive trend toward multiple drug resistance has now been documented.[6] Risk factors associated with transmission of MRSA within the community include crowded living conditions, shared bathing facilities, and participation in contact sports.[33] Over the past decade, niche drift has occurred, with the archetypal hospital strains "escaping" into community circulation, while community-onset strains have become endemic in some hospitals as nosocomial pathogens.[72,76]

Overall, isolation of MRSA from small animal infections remains rare compared to MRSP and MRSS, with some geographical differences *(a table listing published reports will to be added at the time of first revision)*. In North America and Europe, the dominant strain types of MRSA that are carried by (and infect) dogs and cats appear to reflect the prevalence of lineages successful within the human population in the particular region or country.[42,77-79] Unfortunately, these often are the strains that express the most extensive MDR. The true prevalence of MRSA infections in domestic pets within the community is difficult to estimate, as reports have been hospital-based and national population-based surveillance is not performed in pets. An excellent review of the genomic structure and epidemiology of veterinary-sourced MRSA strains is available.[79]

Methicillin-resistant *S. pseudintermedius* (MRSP):

Over the past decade, MRSP has emerged as a clinically important pathogen which causes treatment-resistant infections of dogs and cats.[3,4,37,80] Like HA-MRSA strains, most MRSP isolates co-express resistance to several other classes of antimicrobials, such as the fluoroquinolones, macrolides, tetracyclines, and aminoglycosides.[3,4] Currently, it is common to isolate MRSP that is susceptible to very few antimicrobials, with susceptibility only to amikacin, rifampin, vancomycin and linezolid being a widely encountered pattern. This type of antibiogram presents a true therapeutic dilemma, due both to potential for drug toxicities (amikacin and rifampin) and ethical use considerations (vancomycin and linezolid).

Because MRSA evolved with a clonal population structure and global dissemination of specific clones occurred through the years, it was hypothesized that MRSP isolates would also be highly clonal. Studies of the population genetic structure of *S. pseudintermedius* infection isolates obtained from animals in North America, Europe and Japan have indeed proven them to be highly clonal.[47] Two major clonal lineages have disseminated throughout Europe [Sequence Type (ST) 71], North America (ST 68), and Japan (ST 71), and other less common clonal lineages may be emerging.[50,81] Sequencing of the *mec*A gene has revealed a high degree of homology (95-100%) with the *mec*A gene of *S. aureus*, suggesting horizontal transfer of the gene or acquisition from a common source (e.g. CoNS).[47] The structure of the MRSP phylogenetic tree suggests that the *mec*A gene has been received by this staphylococcal species on multiple occasions and on several different continents.[47]

Methicillin-resistant *S. schleiferi* (MRSS):

In humans, *S. schleiferi* infections appear to be rare. The coagulase-negative variant of *S. schleiferi* is most commonly associated with disease, causing primarily post-surgical skin and soft-tissue infections, while reports of infection by the coagulase-positive subspecies remains very rare (reviewed by Cain).[82] In dogs, both subspecies are commonly associated with skin and ear canal infections, and statistically associated with prior antimicrobial use or recurrent pyoderma.[39,58] Isolation of *S. schleiferi* from pyogenic infections of cats remains exceedingly rare.[3,29] While both subspecies have been isolated from the healthy skin and ear canals of dogs, this remains a rare finding, and the true natural reservoir for *S. schleiferi* remains in question (although it is likely the dog).[23,29,30] The prevalence of MR in *S. schleiferi* clinical isolates is high, and reported to exceed 50% within two veterinary teaching hospitals in the USA.[39,83]

Not unlike MRSA and MRSP, methicillin-resistant *S. schleiferi* is evolving within a clonal population structure. A limited number of strain types, as defined by pulsed field gel electrophoresis, were identified in a collection of 161 clinical isolates that were submitted to a clinical microbiology lab in the USA between 2003 and 2007.[39] In a follow-up report from the same laboratory, it was noted that the population had undergone further periodic selection (reduction of dominant strain types) to three major clonal groups, during the period of 2008 and 2013.[84] A global survey and comparison of *S. schleiferi* strain types has not been reported.

For more detailed information on these three MRS pathogens, the reader is referred to several excellent reviews on the topic.[7,40,79,83] Table 1 provides a summary of recent studies evaluating the prevalence of MRS and methicillin-susceptible staphylococci among dogs and/or cats in hospital and community settings. These data suggest potential regional, temporal, and host species and contextual differences in animal carriage rates.

Laboratory identification of MRS:

S. pseudintermedius has traditionally been distinguished from *S. aureus* based on colony appearance on blood agar and phenotypic tests.[40] Phenotypic identification of *S. pseudintermedius* has been complicated by the recent taxonomic changes, since this species cannot be easily distinguished from the other members of the SIG, *S. intermedius* and *S. delphini*, on the basis of simple and readily available phenotypic tests.[40] Molecular diagnostic methods based on polymerase chain reaction (PCR) are recommended for accurate species identification of coagulase-positive

staphylococci, including *S. schleiferi* subsp. *coagulans*.[85] Proteomic mass spectrometry (MALDI-TOF or matrix-assisted laser desorption/ionization time-of-flight) is a valuable cost-effective, rapid and highly accurate alternative to PCR, provided the database has been refined by strict quality control protocols.[86,87] The great limitation of this technology is the very high up-front cost of purchasing a MALDI-TOF instrument, which implies a high throughput work load to amortize the costs. MALDI-TOF mass spectrometry can be used to identify any bacterial species, including CoNS, provided that the database has been validated for the species of interest. This condition may explain the discrepancies between the studies that have assessed the suitability of this technology for species differentiation within the SIG.[86,87] Indeed, a significant improvement of the SIG identification score values was achieved in one of the studies by refining the original database provided by the manufacturer of one of the two MALDI-TOF instruments available in the market.[88]

PCR amplification of the methicillin resistance gene *mecA* or commercial agglutination tests designed to detect its gene product (penicillin-binding protein 2a, PBP 2a or PBP 2') are presently regarded as the gold standards for identification of methicillin resistance.[89] One of these two methods should be used to confirm presumed MRSA, MRSP or MRSS detected by oxacillin or cefoxitin susceptibility testing.[90] The cefoxitin minimum inhibitory concentration (MIC) is a poorer predictor of methicillin resistance than the disk diffusion test for staphylococci other than *S. aureus*.[91] While for *S. aureus* the cefoxitin disk test is equivalent to oxacillin MIC test, the use of cefoxitin as a surrogate for MRSP detection by disk diffusion is controversial[92-94] and not recommended currently by Clinical Laboratory Standards Institute (CLSI). This controversy may be explained by differences in media used in the different studies and should be investigated further. Strains that are oxacillin/cefoxitin-resistant and *mecA*-positive or PBP 2a-producing should be reported as resistant to all penicillins, cephalosporins (except anti-MRSA cephalosporins), carbapenems and cephems regardless of the *in vitro* susceptibility test results obtained with these agents.[90] This so called "expert rule" was originally established for MRSA to minimize very major errors of antimicrobial susceptibility testing (i.e. resistant strains reported as susceptible) since MRSA infections generally respond poorly to β-lactam therapy, even though MRSA strains may display *in vitro* susceptibility and could erroneously be reported as susceptible to β-lactam agents. The latter phenomenon is due to poor *in vitro* expression of *mecA* in the presence of β-lactams other than oxacillin and cefoxitin, which are used as surrogate drugs for this reason. It should be noted that this expert rule has never been validated for MRSP and MRS other than *S. aureus* and *S. lugdunensis*, which display significantly lower oxacillin MICs compared to the two latter species. This difference is reflected in the oxacillin resistance breakpoints for *S. aureus/S. lugdunensis* (>2µg/mL) versus all other *Staphylococcus* spp. (>0.25 µg/mL).[91]

Therapeutic considerations for MRS infections:

Topical therapy:

Topical therapy, using antibacterial agents with proven anti-staphylococcal efficacy, is the recommended treatment modality for any surface and superficial pyoderma involving MRS, particularly those with localized lesions, and for otitis and superficial wound infection. The skin is easily accessible by topical treatment and antimicrobial formulations for use in small animals are available in most countries. A systematic review of topical therapy for canine skin infections concluded that

evidence from randomized controlled trials was sparse on topical treatments but that good evidence supported the use of chlorhexidine and to a lesser extent of benzoyl peroxide in bacterial skin infections.[95] This review had included studies on canine pyoderma irrespective of methicillin-resistance amongst staphylococcal pathogens and an extrapolation of results is therefore limited. However, minimum inhibitory concentrations (MICs) reported for MRS isolates from pets in North America, Europe and Asia have so far remained low, likely to be exceeded by drug concentrations achievable with topical application. Amongst the almost 200 MRSP included in recent *in vitro* studies, low MICs were found for chlorhexidine (≤ 16 µg/mL), miconazole (≤ 2 µg/mL), fusidic acid (≤ 2 µg/mL), mupirocin (≤ 0.5 µg/mL) and polymyxin B (≤ 4 µg/mL); only one isolate in a collection of 49 showed and MIC of 16 µg/mL to fusidic acid.[96-100] In the three studies that included MRSA isolates from pets, MICs were at least one dilution higher than for MRSP with individual outliers of MICs exceeding 256 µg/mL fusidic acid (6 of 102 isolates).[96-98]

Topical therapy should be used as the sole on-animal antibacterial treatment for surface and superficial infections whenever a pet and owner can be expected to be compliant. Although dermatology texts still recommend systemic antimicrobial therapy for superficial pyoderma with or without added topical medication, this recommendation can be challenged at times of increasing antimicrobial resistance. Newer studies have provided evidence that topical therapy as the sole antibacterial treatment can be effective in superficial pyoderma, providing opportunity to reduce the need for systemic therapy in some cases. Chlorhexidine and benzoyl peroxide shampoos, resolved or substantially improved clinical signs within three weeks in the majority of dogs with MSS superficial pyoderma.[101,102] Similarly, good response to topical therapy alone and no adverse effects were reported in 19/28 dogs with MRSP pyoderma and in all 14 dogs with MRSP pyoderma treated topically in other case series.[80,101,102] Furthermore, the efficacy of a twice weekly chlorhexidine shampoo combined with daily chlorhexidine spray was shown to be comparable to oral amoxicillin-clavulanate in a recently published four-week comparative study in 51 dogs.[103]

While the argument in favor of topical antibacterial therapy is convincing, the choice of drug, particularly in creams, gels and ointments, is more complicated. Geographical differences in availability and authorization for different species exist. and in view of the potential for transmission of staphylococci between humans and animals, antimicrobial choices for treatment of animals need to take into account regional prescribing recommendations in veterinary and human medicine. Concern over resistance to fusidic acid, mupirocin and chlorhexidine exists and resistance genes and increasing MICs in staphylococcal isolates have been described in isolates from humans and animals.[98, 104-107] However, the clinical relevance of currently known resistance markers and of higher MICs remains unclear for topical drug application and clinical treatment failure of topical anti-staphylococcal therapy has not been conclusively reported, to the knowledge of this committee.

Fusidic acid is included in different topical formulations (gels, ophthalmics, otics) and approved for use in dogs in several European countries and in Canada but not, for example, in the U.S. It is also available as an anti-staphylococcal ointment for use in humans in Europe, Canada, Australia and countries in Asia, but also not in the U.S., and is available for systemic use in humans on both continents. In contrast, mupirocin is approved as an antibacterial ointment formulation in the U.S. for use in dogs but in most European countries only for use in humans as treatment of bacterial skin infections and as the most frequently prescribed antibiotic for MRSA

decolonization.[108] In the UK, the British National Formulary recommends that mupirocin should be reserved for the eradication of nasal MRSA carriage in hospital patients and staff.[109] Mupirocin is not used systemically so that *in vitro* resistances may be less relevant as high drug concentrations are likely to be achieved at the site of infection or at carriage sites. In fact, previous treatment failures could so far be linked to environmental contamination or vector transmission, although caution should be used.[104] For fusidic acid though, topical therapy has been associated with the emergence of strains showing high fusidic acid MICs and which may therefore fail to respond to systemic treatment in humans.[110] These differences in use and licensing between countries is unfortunate at a time when intercontinental travel of people, pets and their staphylococci continues to increase. However, while discussion should be encouraged in this area, only products approved for the respective species in each country should be used in the interest of patient safety.

Despite the absence of reports on clinical treatment failure of topical anti-staphylococcal treatment so far, monitoring of MICs, clinical efficacy and further evaluation of topical treatment alternatives[111,112] such as hypochlorite (bleach), Manuka honey and of synergistic combinations is warranted.[113,114] For MRS infections involving biofilm producing strains (for example, around lip folds or implants), additional measures to improve efficacy of topical antibacterial agents may be needed. In addition, constant vigilance of owner compliance is indicated.

Systemic therapy:

For deep pyoderma and for widespread or severe superficial infections and in animals that are not amenable to topical therapy, systemic treatment is indicated. Basic principles of responsible use of antibacterial drugs apply to MRS as for any other bacterial infections. For comprehensive information on treatment of canine staphylococcal skin infections, irrespective of methicillin-resistance, readers are referred to two recently published guideline documents, both available online with free open access. While MRS infections are mentioned, they are not specifically discussed. One document, authored by a group of veterinary dermatologists, addresses diagnosis and treatment of canine bacterial skin infections and classifies drugs into first and second-line antibiotics.[17,115] The other represents a consensus by members of the Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Disease (ISCAID), focuses on management specifically of superficial bacterial folliculitis and groups antimicrobial drugs into first and second tier categories.[18] Both include discussion of empirical and culture-based drug choices, adverse effects and dosage recommendations for antimicrobial drugs.

Efficacy of systemic antibacterial therapy for MRS infections depends predominantly on susceptibility of the organism but will also be determined by correct drug administration including accurate dosing, owner compliance and clinical variables such as severity of disease and causative and concurrent diseases. Due to the extensive multidrug-resistance associated with all MRS, treatment choices for systemic therapy are substantially limited. Information from a recently published systematic review of evidence for systemic antimicrobial treatments in superficial and deep pyoderma are not applicable as no known MRS were included in the reviewed studies.[116]

Susceptibility test results should always be available to make treatment decisions once MRS have been identified. However, if MRS is only suspected, for example following previous infections or based on cytological evidence of infection after antimicrobial therapy,a careful, susceptibility test-based approach is indicated to

ensure best use of the remaining effective agents. This applies even though trends of susceptibilities may be known in some regions – at least for the most successfully spreading lineages. For example, for the treatment of the currently dominant human health-care associated MRSA CC22 which is also the MRS lineage most frequently isolated from pets in the US and the UK, tetracyclines and trimethoprim-potentiated sulfonamides remain good treatment choices based on *in vitro* data and clinical case reports.[117] Amongst MRSSc, susceptibility to tetracyclines and trimethoprim-potentiated sulfonamides had remained in over 80% of isolates as shown in large retrospective studies.[3,39] For MRSP though, individual susceptibilities are infrequent and unpredictable.[3,81,118] In fact, molecular studies have shown that the presence of individual resistance genes can vary even on a single mobile genetic element and within the same lineages.[79,119]

Amongst antimicrobials for which *in vitro* testing has shown susceptibility of a particular isolate, the choice will be based on clinical characteristics. No single drug has been shown to be better than another in a recent Cochrane review on antibiotic treatment of MRSA wounds in humans.[120] Since identification of MRS requires laboratory testing, at least a routine susceptibility profile should always be available with each isolate. If this initial report includes susceptibilities to drugs that are available and licensed for the species, these should be considered first. Additionally, preference should be given to agents with a narrow anti-staphylococcal spectrum to considerations of safety and patient-characteristics such as previous adverse drug reactions, concurrent disease, practicalities in dosing and cost as for other drugs. Specific points to consider for licensed drugs in the context of MRS are:

- Beta-lactam antibiotics should not be used for MRS infections, irrespective of the susceptibility report.[90] Although third generation cephalosporins have a broader spectrum of efficacy than first generation cephalosporins, they do not have efficacy against MRS as shown for cefovecin[121] and cefpodoxime.[122]
- Care is needed when interpreting clindamycin susceptibility as inducible resistance has been reported in MRSA and MRSP associated with certain sequence types[123] Erythromycin-clindamycin-D-zone testing is recommended prior to treatment to avoid treatment failure, particularly with MRSA.[124L]
- Resistance to the tetracyclines is mediated by four different genes, and the genes most commonly expressed by *S. pseudintermedius* are *tet*(M) and *tet*(K). Strains which possess only *tet*(K) maintain susceptibility to minocycline but not to other tetracyclines. The newly approved canine breakpoints for doxycycline[125] are a reasonable surrogate for minocycline susceptibility.[126] Tetracycline may be used as a surrogate for testing susceptibility to doxycycline, but canine specific MIC or disc-diffusion breakpoints should be used.[125]
- Where possible, fluoroquinolones should be avoided for empirical therapy when an MRS is suspected. For the first-generation fluoroquinolones in particular, the disparity in resistance rates between MRSP and methicillin-susceptible *S. pseudintermedius* (MSSP) is striking,[3] and fluoroquinolones have been identified as a major driver for methicillin-resistance in staphylococci.[127] However, this risk needs to be balanced for each patient with the safety profiles of the other drugs available according to the antibiogram.

When no susceptibilities to clinically relevant, routinely used and licensed antimicrobials are reported, extended resistance testing needs to be requested from

the laboratory. Agents then to be considered and for which some information on treatment of canine MRS infections is published.[128,129]

It is important to remember though, that the majority of antimicrobial drugs mentioned here are listed as critically important antimicrobials (CIA) for human medicine in the most recent, third revision of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR).[130] This does not just apply for drugs which are agents not widely approved for veterinary use. Even those approved in many countries for use in pets such as amoxicillin, the fluoroquinolones and the third generation cephalosporins (cefovecin, cefpodoxime) are classified as CIA.(Table 2) Of the antimicrobial agents frequently used in small animal practice, only first generation cephalosporins (e.g. cephalexin, cefadroxil), clindamycin and lincomycin, fusidic acid, the tetracyclines and sulfonamides are included in the second category of highly important for human medicine.

For the glycopeptides (vancomycin, teicoplanin, telavancin), linezolid (oxazolidinone) and potentially new compounds in the future, this group of authors recommends implementation of a restriction-of-use protocol as already in place at one of the authors' institution.[131] Briefly, prescriptions would be considered appropriate after discussion with a specialist experienced in treatment of infectious diseases, after it could be shown that the patient's infection requires systemic therapy, is life-threatening but with a reasonable chance for survival following treatment and when *in vitro* susceptibility had been shown for the relevant pathogen without other treatment options available based on susceptibility testing and patient's medical circumstances. Glycopeptides and linezolid are drugs indicated in human medicine for the treatment of serious infections due to Gram positive bacteria (e.g. peritonitis in peritoneal dialysis patients, endocarditis) or for surgical prophylaxis if there is a high risk of MRSA. Vancomycin and teicoplanin given orally (poor enteric absorption) are further used in the treatment of *Clostridium difficile* infection. Recently, increasing vancomycin resistance amongst enterococci (VRE) have become a major concern in human and veterinary medicine and individual isolates of vancomycin-resistant MRSA have also been reported.[132-134] This group of drugs should not be needed following the conditions outlined above and should be reserved for human medicine.

Some general recommendations on duration, dosage and combination with topical therapy apply for MRS infections in the same way as for MSS infections. Frustratingly, good evidence for recommendations on treatment duration is sparse and specific dose assessment for treatment of MRS has not been published. In the absence of such data, current published advice on the duration of treatment (three weeks for superficial pyoderma or one week beyond clinical resolution and four to six weeks for deep pyoderma or two weeks beyond clinical resolution) should be adhered to.[17,18] The combination of systemic therapy with topical antibacterial treatment is recommended whenever possible to reduce environmental contamination and the risk of transmission to other hosts.

Outcomes of treatment for staphylococcal infections:

Veterinary case-control studies have shown that methicillin-resistant staphylococcal infections do not necessarily have less favorable outcomes than methicillin-susceptible infections in dogs and cats, as long as a safe antimicrobial alternative is available for treatment.[38,39,80,135] Treatment outcome of MRS infections in small animals appears to depend on restoring the skin barrier function and removal

of implants combined with antibacterial therapy, either by topical, systemic or intralesional route. However, when inserted into a highly virulent strain, extensive antimicrobial resistance may greatly complicate therapeutic interventions and could ultimately worsen outcome if resistance is not promptly identified and proper therapy instituted.

Outcome of MRSA infection in comparison to MSSA infection is frequently studied in human hospitals due to concern about increased mortality from drug-resistance but also to assess the impact on healthcare cost. While some of the more recent reports appear to document an increased risk of mortality in certain patient groups with MRSA,[136] conflicting results remain, likely due to the heterogeneity of MRSA infections (blood stream infections vs. skin and soft tissue infections) and healthcare provision and bias from patient characteristics (age, co-morbidities). In a case series of eleven dogs with MRSA surgical site or skin infection, systemic antibacterial therapy based on susceptibility testing, improved or resolved the infection in nine of the eleven dogs; one dog had been euthanized with radiographic evidence of osteomyelitis, the other lost to follow-up.[137] In a multi-institutional retrospective case-control study of 40 dogs with MRSA infection and 80 dogs with MSSA infection, no significant differences in duration of hospitalization or euthanasia rates were found. Most infections were limited to the skin, with no difference in body tissue/organ distribution between the groups.[38] In a small retrospective case-control study of 11 cats with MRSA and 29 cats with MSSA, no statistically significant differences between groups were detected in signalment or mortality, nor subjective differences in clinical signs/morbidity and response to therapy based on culture-directed antimicrobial therapy.[135]

In regards to *S. pseudintermedius*, a retrospective comparison of medical records of 123 dogs with MSSP pyoderma and 93 dogs with MRSP infections showed no difference between groups with regard to outcome although individual MRSP infections took longer to resolve.[80] Similarly, of 12 pets with MRSP infection, clinical signs resolved or markedly improved in 11 patients, again, one dog was euthanized with signs of osteomyelitis after chronic otitis media.[118]

It may be therefore concluded, based upon these limited clinical data, that MRS are generally no more virulent than MSS and not associated with a worse outcome. The findings of clinical reports are compatible with the lack of genetic markers for invasive behavior so far identified in staphylococci. A large microarray study previously compared invasive clinical *S. aureus* isolates with nasally carried strains from humans and concluded that the outcome of the patient-staphylococcal relationship was strongly dependent on host factors.[138] Similarly, known *S. pseudintermedius* toxin genes such as *siet* and *luk I* have been described in MSS and MRS with no known association with specific disease or prognosis.[139,140,141]

In summary, with the potential for selection, referral, and many other study design biases in mind, it has to be concluded that there is little evidence for a difference in outcome between MRS and MSS infections in animals and that the prognosis for MRS skin infections in pets is good, depending on underlying causes.

“Decolonization”:

Once MRS infection has resolved, humans and animals can continue to carry MRS at skin and mucosal sites with associated risks for the patient and others, either via direct contact with the carrier or via environmental contamination.

In a medical context, the term “decolonization” is most commonly used to describe

the eradication of MRSA from skin and mucosal carriage sites by antimicrobial treatment. Alternatively, decolonization may occur naturally if a patient loses MRSA carrier status without medical intervention over time.[142]

MRSA decolonization in human medicine:

The efficacy of a combination of decolonization treatment with MRSA surveillance sampling, mostly prior to hospital admission, in the prevention of healthcare-acquired infections was recently supported by good evidence from a systematic review of 83 European studies published between 2000 and 2012.[143] However, decolonization remains a controversial topic in human medicine as efficacy is often short-term, best protocols are not established, ethical concerns remain about the use of antimicrobial agents in essentially otherwise healthy carriers and adverse events and development of resistance during therapy has been reported.[144] Systematic assessment of decolonization regimes include variation in outcomes assessed (e.g. negative culture at different time points, effect on bacteremia rates or surgical site infections), the competing effects of additional environmental hygiene interventions, differences in transmission pathways between settings and importantly, the effect of MRSA prevalence on screening, isolation and decolonization.

A justification for decolonization is supported by the finding that 80% of *S. aureus* bacteremia cases in humans were shown to involve genetically identical isolates as those carried by the patient nasally on admission, suggesting that carried strains are well adapted to their host and thus, with an advantage for proliferating to infection should the opportunity arise.[145] Even though data on the impact of pre-operative nasal MRSA carriage on post-operative MRSA infection are conflicting,[146,147] the concept is plausible that eradication of MRSA carriage can reduce the risk of MRSA infection from endogenous MRSA but not the transmission of MRSA through in-contact people or environmental contamination.

Decolonization in dogs:

In dogs, no studies have assessed the need or best protocols for decolonization of MRS carriers. However, a small number of longitudinal studies of MRSP carrier dogs are reported and similarities between human *S. aureus* carriage and canine *S. pseudintermedius* carriage exist that may allow comparison and possibly support or refute a case for screening and decolonization or at least conclusions on hygiene recommendations.

Mucosal *S. pseudintermedius* carriage appears to play a similar role in canine skin infection that described for *S. aureus* blood stream infection in humans.[145] In dogs, 80% of *S. pseudintermedius* carriage isolates from mucosae were genetically identical to isolates from pustules of the same dog.[148] For MRSP in particular, a prospective multicenter study of 549 dogs showed that MRSP carriage on admission predisposed to post-TPLO surgical site infection with an odds ratio of 6.72.[149] MRSP carriage appears to be a common sequel to infection as shown through longitudinal sampling after resolution of infection. In 42 dogs sampled after clinical resolution of their MRSP infection, MRSP carriage was detected in 61.9% between 3 and 15 weeks after initial presentation[37] and persistence of carriage could be shown to last for up to 11 months following clinical cure of infection.[150]

What are the risks associated with carrier dogs?

MRS colonized or contaminated pets can pose a risk to susceptible in-contact people and animals as staphylococci typically reside on surface sites ideally suited to

transmission by direct contact, e.g. licking.[151] Staphylococci adhering to corneocytes[152] and can also be transmitted via indirect routes through desquamation into the environment, enhanced by their ability to survive on surfaces for many months.[153,154] For MRSA, there is ample, although still indirect, evidence for transmission from pets to people[104,154-156] via either or both direct and indirect routes; transmission of MRSP from pets to people has been reported less frequently. However, environmental MRSP contamination was associated with the presence of infected or colonized index dogs in two similar studies where MRSP-infected dogs, in-contact animals and people and environmental sites were sampled over time.[157,158] The results of both studies indicated that MRSP could be easily transmitted to dogs but not to people. This finding is further supported by *in vitro* adhesion tape corneocyte assays which showed that *S. pseudintermedius* adhered better to canine corneocytes while *S. aureus* showed preference to human squames.[152]

Natural decolonization:

Natural decolonization, i.e. the loss of MRS from carriage sites without on-animal treatment, occurs likely due to competition within the bacterial microflora. Multidrug-resistance in a bacterial isolate improves survival chances at times of drug treatment. However, this advantage fades when treatment stops and carriage or expression of resistance genes becomes a metabolic burden for the multidrug-resistant strain competing for its niche. Such fitness cost in exchange for drug resistance has been well documented for *S. aureus* and the emergence of different successful MRSA lineages over time.[159-162]

Evidence for natural decolonization is difficult to find though as environmental contamination is closely interlinked but more difficult to assess. Carriage swabs, taken at a single occasion and processed by selective culture for the MRS target organism, will identify colonizing bacteria but also transient contamination of carriage sites, either from the environment or contact with infected sites. Such transient carriage was illustrated in an older study where human hospital nurses were sampled for MRSA carriage immediately following a duty shift and of 13 carriers, 12 were found negative the following morning before duty.[163]

Natural decolonization was also demonstrated in healthy MRSA carrier dogs kept in regularly cleaned environments. Ten of a total of 129 dogs at a rescue facility were found positive for MRSA at mucosal and skin carriage sites while all 16 companions sharing a kennel with one of the carriers were negative. All carriers sampled negative within two weeks. Kennels were cleaned twice and disinfected once daily.[164] In a cross-sectional study of dogs and cats that resided with human MRSA patients, the odds or MRSA isolation from “carriage” sites decreased by xx.x for each day that pet sampling was delayed after the person started antimicrobial therapy.[32] These studies suggest that dogs do not support MRSA carriage for long periods, at least in clean environments. MRSP carriage on the other hand, was shown to persist for over 12 months after infection had resolved albeit in household settings without special cleaning interventions.[37,150,157]

Would decolonization with antimicrobial agents work?:

Resolution of MRS infection is a pre-requisite of decolonization as carriage sites will otherwise be contaminated by pathogens. MRSP decolonization with systemic therapy, even using agents to which the MRSP shows *in vitro* susceptibility, is unlikely to be effective based on the persistence of MRSP carriage after successful treatment and resolution of pyoderma shown in two studies.[37,150] Decolonization

using topical antimicrobial agents can be effective though, at least for short periods. Significant reductions in colony-forming units of *S.(pseud)intermedius* from treated mucosal carriage sites and untreated cutaneous have been seen following twice daily application of fusidic acid in a 1% viscous eye drop formulation.[165] Mucosal treatment reduced bacterial counts typically from multiples of 10^3 to less than 10 colony-forming units per swab at two days after treatment and reduced *S. (pseud)intermedius* counts were still seen three weeks after cessation of fusidic acid therapy. Provided good compliance, the same effect may be expected against MRS carriage in dogs as minimum inhibitory concentrations of antibacterial agents available for use in pets tended to be low.

Conclusions on decolonization:

There is currently not enough evidence to recommend routine decolonization of MRS carrier animals. However, MRS carrier dogs pose a risk to susceptible in-contact humans and animals through direct contact and contribute to MRS contamination of their environments. Natural decolonization should be supported through rigorous hygiene measures, where possible combined with temporary isolation to ease cleaning and disinfection. Some clinicians recommend follow-up sampling of carriage sites to identify persistent carriage and the need for further hygiene measures, whereas others do not due to lack of evidence to support the utility of interventions. There is no evidence on when MRS carriage can be considered resolved.

Methods for establishing strain concordance in a proposed "outbreak":

Molecular characterization of staphylococcal strains is a widely-used research tool that can provide information about genetic relatedness, evolutionary history, virulence factors, mechanisms of antimicrobial resistance and other properties. It can be used as part of molecular epidemiological investigation for various reasons, such as determination of whether a group of infections are potentially linked or to determine whether infections are caused by a recognized or new strain. A range of methods is available and selection of methods for a particular investigation is based on a combination of factors, such as availability, cost, throughput and discriminatory power.[1-5 166-170] Common methods are outlined in Table 3. As a general trend, access to cheap Next Generation Sequencing (NGS) has determined a gradual shift from DNA band-based methods such as PFGE to sequence-based methods such as MLST and *spa* typing.

While typing methods are widely available, molecular characterization typically provides limited clinically relevant information and typing of isolates is usually reserved for rare situations such as outbreaks. Typing is an important component of outbreak investigation, but even within outbreaks, the usefulness of typing may be limited, depending on the organism, epidemiology, typing method(s) and investigation goals. In the context of investigation of a potential outbreak, identification of different strains can provide assurance that a single point-source is not present. Finding indistinguishable isolates according to one or even two typing mechanisms *suggests* that they *might* be linked, but this depends to a large degree on the discriminatory power of the typing method. Typing alone may not be definitive,[171] although advances in typing methods, particularly whole genome sequencing, increase the potential yield of molecular investigations. Whole genome sequencing currently is used almost exclusively in the research setting as real-time analysis, necessary for clinical application, is difficult and resource-intensive. As ease and speed of

sequencing and data analysis improve, this will likely become more clinically applicable in the near future.

Some pathogens are relatively clonal, with a small number of discernible strains present in a circulating area. MRSP exemplifies this situation, with a small number of clones, predominating internationally and locally.[166,167,172] Thus, identification of the same strain in a group of cases from a clinic could represent a true outbreak or simply the 'background' molecular makeup of MRSP in the region. Typing can provide useful data, but those data must be evaluated with an understanding of the typing method (e.g. what it is assessing, discriminatory power) and with corresponding epidemiological data.[173] From a clinical standpoint, the potential actions that would result from obtaining typing data must also be considered. While it is possible that identification of a clonal outbreak of a *Staphylococcus* would lead to a specific infection control intervention, this would be uncommon. Most often, typing provides interesting data about the epidemiology and ecology of the organism, but does not have any impact on patient- or even clinic-level management. Molecular characterization is therefore typically reserved for research studies. If an ongoing, large or unusual cluster of staphylococcal infections is occurring within a clinic, there might be a benefit to characterization of isolates; however, that should only be considered as part of a broader infection control investigation, typically with the involvement of infectious disease specialists.

Questions often arise about characterization of isolates from animals when there may be a corresponding human infection, typically involving MRSA. Characterization of human and animal isolates in those situations is interesting but provides little practical information. From a logistical standpoint, there can be challenges in securing both human and animal isolates and having them transferred to the same laboratory. This may not be required for all methods, since some (e.g. spa typing) are amenable to accurate inter-laboratory comparison. However, more subjective methods such as PFGE should be performed side-by-side. Even if isolates are obtained and able to be tested, the relevance of the results is usually unclear. For example, finding the same strain of MRSA in a person and pet is interesting, and supports interspecies transmission. Yet, it is difficult to elucidate direction of transmission, or even if there was transmission between those individuals.[32] It is possible that both human and pet could be exposed by another unknown individual (human or animal) or via a shared environment. Whole genome sequencing can provide important insight into some outbreaks, where subtle changes in the pathogen over time can be used to elucidate potential sources and directions of transmission. This is most applicable to outbreaks or high endemic infection rates that occur over time.

Veterinary Hospital Infection Control:

There is an ever-present risk of MR staphylococcal exposure for patients and humans in a veterinary hospital. As opportunistic pathogens that are not uncommonly found as part of the commensal microbiota, every human or animal poses some risk of introducing an MR *Staphylococcus* into the facility. Routine infection control practices are the cornerstone to control of MR staphylococci. This involves a collection of procedures and practices designed to reduce the risk of exposure to various pathogens. "Good routine practices done consistently and well" should be the emphasis. Design and implementation of an infection control program is beyond the scope of this document, but some good general resources are available.[174-176] Selected areas are briefly outlined below.

Personal protective equipment:

Personal protective equipment (PPE) is designed to protect the wearer, preventing contamination of underlying skin and clothing, as well as protect patients from exposure to contaminated body surfaces and clothing.[177] Routine personal protective equipment is ideally a laboratory coat over street clothes or scrubs, as the laboratory coat provides full torso and arm coverage and can be changed easily. Scrubs are often worn by veterinary personnel but should not be the outer PPE layer because they do not provide arm cover and are not as easy to change. When possible, coats and scrubs should be laundered in hospital rather than at home to reduce microbial contamination and take-home exposures.[178] Ties, scarves, lanyards and other accessories that may become contaminated should be covered by outer PPE or not worn.[179]

In some situations, enhanced PPE may be required. This would include one or more of the use of a gown or outerwear layer that is only used for one patient, gloves, mask, eye protection or face protection.[180] No data exist regarding optimal PPE practices for handling animals infected with MR staphylococci. However, the use of some degree of enhanced precautions to reduce contamination of clothing and skin is reasonable. Typically, this would consist of a gown or dedicated laboratory coat and gloves. Gloves can be effective additional barriers but are often misused.[181] Common errors with glove use are continuing to wear the gloves after the patient contact and contaminating various surfaces, as well as failure to perform hand hygiene after glove removal. Masks are occasionally used in human healthcare when managing MRSA-infected patients, mainly to reduce hand-nose contact (and the associated risk of becoming colonized). The same could be considered in veterinary hospitals, particularly with personnel who frequently touch their face inadvertently during patient care. However, masks are rarely used or indicated.

When to use routine versus enhanced practices has not been well defined in the context of veterinary dermatology. The combination of a high prevalence of MR staphylococcal infection or colonization in the caseload and frequent contact with animals at increased risk of staphylococcal infection (e.g. diseases that affect the normal skin barrier) presumably creates abundant risk of MR staphylococcal transmission in many dermatology practices. In areas where the prevalence of MR staphylococci is high, consideration should be given to enhancing routine PPE, such as changing laboratory coats between patients and wearing gloves for any contact with potentially infected or compromised skin.

Hand hygiene:

Hand hygiene is perhaps the simplest and least expensive infection control practice, but it also tends to be poorly used.[181] The role of hands in transmission of MR staphylococci between patients or as a source of infection of personnel is unknown, but probably substantial. Proper hand washing and drying[182], or use of an alcohol based hand sanitizer,[183] can effectively reduce staphylococcal skin contamination and therefore presumably reduce the risk of MR staphylococcal transmission. The actual efficacy of hand hygiene is unclear, even in human medicine, because it is exceptionally difficult to differentiate the role of hands versus other sources, but hand hygiene compliance is a major component of virtually any infection control program.

Ensuring adequate numbers, accessibility and stocking (soap, paper towels) of sinks can facilitate hand washing compliance; however, hand washing can be limited

by access to sinks, and adding or repositioning sinks is often cost-prohibitive. Alcohol-based hand sanitizers can be provided to personnel and easily placed or mounted throughout a facility, facilitating access to hand hygiene in all patient care areas. Hand washing should be performed when there is abundant gross contamination (e.g. pus) of the hands, but, otherwise, hand washing and hand sanitizers are essentially interchangeable. Hand sanitizers may be less damaging to the user's skin with frequent use.

MRS patient or carrier? Isolation practices:

Isolation is designed to limit direct and indirect contact between an individual and other individuals, as well as the general environment. It is an effective tool for reducing transmission of various pathogens, including those such as staphylococci that are spread primarily by direct and indirect contact. In human medicine, contact precautions are typically used with MRSA infected individuals. This usually involves housing the patient in a private room, limiting visitation and using enhanced protective equipment for any patient contact. In veterinary hospitals, isolation may involve housing a patient in a dedicated isolation ward or using enhanced precautions in a general ward. While direct and indirect transmission should be able to be effectively controlled in a general ward with isolation practices, physical and procedural separation (isolation unit) is presumed to be more reliable than procedural separation alone. The size of the isolation unit, ability to perform patient care activities in isolation, number of animals with MR-staphylococcal infections and nature of the rest of the hospital caseload (e.g. presence of a large population of high risk surgical cases) impact decisions on whether to house animals with MR-staphylococcal infection or colonization in isolation or wards. Regardless of the location, clear management policies (e.g. cleaning and disinfection, animal movement, PPE) must be available.

Cleaning and disinfection:

Cleaning and disinfection are designed to reduce or eliminate pathogenic burdens in the environment and on equipment.[184,185] Routine cleaning and disinfection practices are the most important part of a comprehensive program. Staphylococci are readily inactivated by routine disinfectants, including those that predominate in veterinary facilities (e.g. quaternary ammonium disinfectants, accelerated hydrogen peroxide). However, cleaning and disinfection are two separate steps, and cleaning is required for effective disinfection. Failure to properly clean a surface can result in ineffective disinfection through inhibitory effects of organic debris (e.g. dirt, hair, pus) and biofilm. Good cleaning will remove the majority of contaminants and prepare the surface for effective disinfection. In addition to a proper surface, adequate disinfection requires an appropriate concentration (dilution) of the disinfectant and the proper contact time, which varies between products. Of note, recontamination following cleaning is typical, which emphasizes the importance for such practices to be conducted on a frequent schedule.

Enhanced practices are sometimes used in response to specific contamination events or cases. Since MR staphylococci are susceptible to commonly used disinfectants, identification of an infected patient does not necessarily mean that a change in cleaning and disinfection is needed. Periodically, MR staphylococci harboring genes (e.g. *nor*A, *qac*A/B) that confer resistance to certain disinfectants may be identified, and such situations may warrant closer examination of disinfection protocols.[186]

If routine cleaning and disinfection are performed properly, no additional work should be needed. This emphasizes the need for a properly-designed cleaning and disinfection program, with documentation of disinfectant practices (product, dilution, contact time), when cleaning and disinfection must be performed, and related basic information. In some situations, changes to the timing of cleaning and disinfection may be indicated, such as performing this immediately after an infected patient leaves the room rather than at the end of the day. Disinfection of items that are not routinely disinfected might also be considered, such as clippers after use on an infected patient. However, since only a potentially small percentage of animals harbouring MR staphylococci are known at the time of examination, focusing cleaning and disinfection (and other infection control practices) on the known cases risks missing a large number of other infectious individuals. This emphasizes the importance of routine, consistent general practices rather than MR staphylococcal-targeted practices.

Identification of infected animals:

Identification of MR staphylococcal infections is important for case management and infection control purposes and this can only be achieved through diagnostic testing. Early identification of MR staphylococcal infections is important, so diagnostic testing prior to empirical treatment is preferred, although the realities of clinical practice can limit testing. Testing should be considered particularly important with serious infections and infections that have not responded to empirical therapy. It should also be strongly recommended in situations where a resistant pathogen is more likely, such as in animals with previous MR staphylococcal infection, recent antimicrobial exposure, recent hospitalization or those that live with a person or animal with a history of MRSA or MRSP infection. Testing of potentially hospital-associated infections is also beneficial to provide important information about endemic rates and to identify clusters of infections as early as possible.

Surveillance:

Related to identification of infected animals is recording of data pertaining to infections. Understanding endemic rates of disease is critical for accurate and prompt identification of 'abnormal' rates, whether it is a gradual change in rate or a sudden high-incidence outbreak.[187]

The most common and practical form of surveillance in veterinary hospitals is passive surveillance. This involves recording (or being able to retrieve) basic data about disease incidence or characteristics (e.g. antimicrobial susceptibility profiles). Understanding the typical incidence of MR staphylococcal infections can be facilitated by central recording of MR staphylococcal diagnoses from routine clinical activities. This can be used to generate information about the baseline/endemic rate, which can be monitored over time. Changes in rates can then be investigated. Antimicrobial susceptibility data can also be monitored to provide guidance for empirical therapy and to detect changes that might suggest a change in the epidemiology of the pathogen in the clinic or region. Use of electronic health records and laboratory software programs for tracking data can enable or enhance these passive surveillance activities. This can be of use for practice-specific decision making, as well as provide data that can be used for broader evidence-based guideline development.

Active surveillance is a more expensive and time consuming method that involves *de novo* collection of data for infection control purposes, such as MRSA or

MRSP screening at the time of admission. Active surveillance is rarely used in veterinary hospitals because of the cost, time commitment, relatively low burden of hospital-associated MR staphylococcal infections and limited evidence of usefulness. Active surveillance might be useful as a periodic surveillance tool to understand the epidemiology of MR staphylococci in a clinic, or in response to an increased incidence of disease or an outbreak, but such situations would be uncommon. Any active surveillance should be designed with the input of a specialist to ensure that useful data are obtained and that resources are effectively used.

Community spaces

Control of MR staphylococci at the community level is exceptionally complicated, in part due to the overlapping human and animal epidemics and shifting epidemiology on both sides. On one hand, limiting further dissemination of important pathogens such as MRSA and MRSP is a laudable goal. On the other hand, if these are carried by even a small percentage (e.g. <1-3%, see Table 1) of healthy individuals, it becomes clear that animals with known infections constitute only a fraction of the pool of potentially infectious individuals. They might pose a somewhat higher risk because of higher staphylococcal burdens at infected sites; however, virtually nothing is known about the relative risk of transmission from healthy versus clinically infected versus recently infected individuals.

It would be logical to consider a few different groups in terms of risk of infectivity. Individual animals at highest risk are those with active MR staphylococcal SSTIs that may be shedding the organism from both the site of infection and colonization sites. The next risk group would be animals with recent infections. Duration of shedding has not been well defined, and appears to differ among staphylococcal species and hosts. In general, it is thought that MRSA shedding is relatively short-term (days to weeks) after resolution of clinical infection,[188-190] while MRSP shedding may be prolonged in some individuals, especially dogs.[150,191,192] The potential for long term (months to years) shedding of MRSP post-infection complicates control measures since no defined period of risk can be given in the absence of testing. Another group would be individuals with known risk factors for MR staphylococcal carriage, such as recent antibiotic exposure, visitation of human hospitals or hospitalization in a veterinary clinic.[189,193-196] Animals in this group could be highly variable, and this variability could mean that the potential risk conferred is best assessed on an individual basis. Beyond these would be the ‘lowest’ risk population, healthy animals with no hospitalization or antibiotic exposure. However, even in this population, MR staphylococcal carriage is possible. Therefore, while some animals likely pose greater risk than others, any community-level contact with an animal is presumably associated with some (albeit low) risk of MR staphylococcal exposure. Further, while the risk posed by any individual animal-animal or human-animal contact is presumably low, there is an accumulating risk of MR staphylococcal carriage with more contacts. More contacts, and more contact with higher-risk individuals presumably increase the risk of community-based transmission. This applies for virtually every other infectious disease and should not itself be taken as an indication of the need for social distancing or contact isolation.

Determination of how to manage community risk is difficult because of a lack of clear data and the subjective (and variable) determination of costs vs benefits. Social aspects of animal-animal and animal-human interaction are difficult to quantify but should not be ignored. Other benefits such as exercise and practical aspects of boarding (day care or longer term) boarding also bear consideration. Further, it is

possible that animals harbor microbes or participate in microbial sharing that increases beneficial bacterial diversity for in-contact animals and humans.[31,197] Case-by-case consideration of the costs and benefits to the individual animal, the animal's family and broader human and animal populations should be performed, as difficult as this may be.

In terms of restriction of individuals conferring risk, the greatest attention should be paid to individuals with active infections, since they likely constitute the greatest risk. Restricting these individuals from contact situations (e.g. dog parks, play groups, competitions, kennels) is logical. How long to do so is unclear, as risk is presumably highest prior to the onset of treatment, with a relatively rapid decline thereafter. Considering the potential duration of treatment of staphylococcal skin infections, restrictions throughout the entire treatment period can become problematic. In lieu of data to guide recommendations, it is reasonable to restrict animals from contact situations until treatment has started and a clinical response is evident. Thereafter, some degree of elevated risk is still presumably present, perhaps more from carriage sites than the infected site. While recently infected animals or those with risk factors for carriage (e.g. recent hospitalization) likely pose additional risk, the costs of restriction may outweigh the benefits, and the presence of an unknown but not insubstantial pool of other MR staphylococcal carriers limits the benefits of restricting this small but known population. Human guidelines for management of community-associated MRSA, even in high risk environments such as childcare or sports teams, do not recommend exclusion of colonized or high risk individuals.[197,198] Instead, they focus on covering infected sites (something that is rarely possible with skin infections in animals) and general personal and environmental hygiene practices.

Correspondingly, management of particularly susceptible individuals that are at increased risk of acquisition of MR staphylococci or increased risk of progression to clinical infection given MR staphylococcal exposure is worthy of consideration. In some situations, a period of increased risk is short and defined, such as after undergoing surgery, having a wound, or being treated with an antimicrobial or short-term immunosuppressive therapy. It is easier to justify short-term restriction such as keeping dogs away from off-leash parks, playgroups or kennels during a defined and short-term period of risk, because the costs may be limited and manageable. When individuals have persistently elevated risk (e.g. uncontrolled inflammatory skin disease, chronic immunosuppressive therapy), the issue becomes more complicated. Overall, the risk of mixing in community settings is presumably low, even in high-risk individuals. Basic practices such as limiting overall dog-dog contact, trying to keep dog-dog contact to defined groups (as opposed to random encounters with a more variable population), avoiding contact with animals that may be at increased risk (something is difficult to identify but possible in some situations) and avoiding contacts during periods of heightened risk (e.g., an atopic flare) are logical but unproven.

In-home mitigation:

Within the community, households have shown the greatest potential, not just as a point of transmission of relevance in a clinical context for both people and pets, but also as a potential intervention point.[33] Exchange of staphylococci between humans and pets, both in the context of recurrent disease and colonization, may be common. Humans, other companion animal household members, and home environments (including pet bedding) have been implicated in or associated with

staphylococcal carriage or infection in dogs and cats.[171,199,200] The potential for transmission of staphylococci among all human and animal members of the household, to home surfaces, and from home surfaces is accepted, although consensus has not yet been achieved regarding how frequently this occurs in the context of causation and the predominant direction(s) of transmission. Although household interventions have been minimally assessed in the literature, certain precautions deserve attention, especially if the household includes immunosuppressed patients.

Hygiene and contact precautions:

Transmission of staphylococci—particularly *S. aureus*—may occur in both directions between owners and their pets; pets typically carry *S. aureus* strains genetically similar to locally dominant human clones,[199-202] Similar relatedness has been identified in pets and owners that are co-colonized with *S. pseudintermedius.*[199,200] Because of this potential, contact isolation strategies (e.g. crating and exclusion from the bedroom) have been recommended to segregate infected or positive pets from other pets and humans.[33] Not only may pets become carriers or colonized with staphylococci once in contact with infected or colonized people or other pets, but their fur (i.e. "petting zone") also may become contaminated, presumably through the hand contact of owners.[189] This suggests an important potential role for good hand hygiene (e.g. hand washing or use of a hand sanitizer) before and after owner-pet contact, although the effectiveness of such strategies has not been formally tested.

Environmental measures:

Despite a growing consensus in the literature that home environments may serve as reservoirs for staphylococci in the context of both human and animal disease, the efficacy of environmental control strategies is largely unexplored in the literature. Laundering, including on normal low-temperature settings, has been demonstrated to reduce *S. aureus* contamination of clothing in the context of hospital settings;[204] laundering of bedding materials in household settings may be beneficial. Household disinfectants (e.g. chlorine and quaternary ammonium-based cleaners) appear to be effective in reducing *S. aureus* contamination from surfaces (reviewed by Davis et al[33]). However, data from hospital settings also suggest that environmental surfaces and clothing may rapidly become re-contaminated following successful treatment.[205,206] Hence, when animals are being treated, concurrent home cleaning may be helpful to prevent re-exposure and recurrence. In some cases of recurrence, addressing human and animal household members also may be necessary, although the human literature demonstrates that adopting a similar approach of household-wide decolonization to reduce recurrence of SSTIs in people has shown weaker benefit than anticipated.[207,208]

Screening of healthy pets and people:

Screening of healthy pets and people for carriage of selected staphylococci (e.g. MRSA or MRSP) can provide interesting information about the epidemiology of staphylococci, as well as interspecies transmission. It is also an area that can be fraught with potential problems, particularly when clear plans for how to access and use the results have not been determined and communicated prior to testing. Testing of clinically normal animals rarely leads to clear and justifiable action. Testing of humans leads to issues of confidentiality, and testing of clinic personnel (especially if

not clearly voluntary and anonymous) could lead to a host of legal problems for clinic management. Testing of healthy individuals, particularly humans, should be a rare event that is based on a specific need and with a clear plan to act on the results.

Testing to identify increased risk in a patient:

Using screening to inform risk profiling among patients has the greatest potential, among all potential scenarios, for widespread adoption. In humans, MRSA screening is used judiciously in certain risk groups to target specific interventions, e.g. patients admitted to the intensive care unit may be screened and MRSA-positive individuals subjected to barrier precautions. Similarly, patients scheduled for orthopedic surgeries may be prescribed decolonization treatment, although evidence of this risk and efficacy of decolonization are variable.209-212[24-27] There is limited corresponding information in veterinary medicine. MRSP carriage has been associated with increased risk of MRSP infection following tibial plateau leveling osteotomy (TPLO) in dogs,213[28] suggesting that screening could be considered in this population and susceptibility results used to guide peri-operative antimicrobial drug administration for MRSP carriers. However, the potential clinical impact of screening has not been investigated and there is limited evidence to identify other high-risk situations that would be accompanied by a potential intervention. As more evidence about risk groups, rapid screening methods and studies of interventions become available, there may be broader use of targeted screening for select, high-risk patients. Currently, the evidence for potential benefit from screening programs is strongest for surgical patients and most limited for dermatology patients.

Testing to identify potential personnel sources of an outbreak:

Screening of personnel has been performed in veterinary clinic or farm MRSA outbreaks.[214,215] However, these investigations were more focused on understanding the epidemiology of MRSA as it emerged in animals rather than as a tool to identify and mitigate an infectious focus. Veterinary personnel are known to be at elevated risk of MRSA and MRSP carriage in the absence of outbreaks,[216-221] and screening results are difficult to interpret in the midst of an outbreak. Finding MRSA or MRSP in personnel could indicate that they were a source of infection, but it could equally indicate they were infected by a patient or coworker, were exposed to a contaminated environment, or were exposed to an unrelated strain outside the hospital setting. Removal of colonized veterinary personnel from patient care duties is not recommended, and attempts to do so could lead to management or even legal challenges for the clinic. Given the importance of good personal hygiene and routine infection control practices at all times (not just during outbreak settings), knowing an individual's status is likely to change a hospital-level approach to infectious disease management. The exception might be in a situation where there is clear evidence of a hospital focus and enhanced control measures have failed to contain the problem. Even then, the confidentiality issues associated with testing and management of a colonized individual complicate testing decisions.

Testing of humans after contact with an infected animal:

Owners periodically raise concerns about their personal exposures to MR staphylococci and request testing for themselves or their families. Any testing would have to be done within the human healthcare system, and discussions of this would be between the individual and their physician. Although the veterinarian could—and arguably should, if indicated—be an integral part of a one health approach to

household-wide interventions, the owner would need to actively involve the veterinarian given privacy laws protecting human health information in many countries. Regardless, consideration of how the results would be handled is important. Without highly discriminatory methods such as whole genome sequencing, combined with repeated sample collection from all individuals over time, standard microbial culture cannot be used to determine if the pet has infected people. If a pet had an MRSA infection and the owner was subsequently identified as colonized, a positive culture would not differentiate pet-to-human transmission from the more likely human-to-pet scenario. Indeed, genetic testing of animal isolates has implicated the human MRSA epidemic of spilling over into the pet population.[201] Testing of a person would only be of relevance in a situation where knowing their MRSA status would impact their medical care, e.g. before the owner would undergo elective surgery or if the owner was particularly susceptible due to a medical condition. Routine decolonization of healthy individuals in the community is rarely indicated, being restricted mainly to situations where there are recurrent infections in an individual or ongoing transmission in a household that is not responsive to other control measures.[199] With that approach, there would typically be no relevant impact of testing owners of MRSA-infected pets.

Testing of pets of owners who have been diagnosed with an MRSA and other MRS infections:

Requests to test pets of infected owners—particularly when an owner has a MRSA infection—is not uncommon, and must be approached with the question 'why'? MRSA carriage can be identified in pets of infected owners,[32,222] but that provides limited useful information for management of MRSA in a household. The vast majority of human MRSA infections are human associated, with exceptions for certain regions, communities, or occupations where livestock- or equine-associated MRSA may be a consideration in people. Thus, finding MRSA in the pet could represent pet-human transmission, but more likely represents human-pet transmission. Since MRSA carriage tends to be short-term in pets[32,188-190,] and there is no evidence that active decolonization is useful or effective in pets, finding an MRSA positive pet in such a household would typically lead to a recommendation to focus on personal hygiene and temporary contact isolation to reduce the risk of transmission of MRSA in both directions. Further, no screening test is 100% effective; screening the most sensitive site, the mouth, was shown to miss up to a third of animals with CoPS and almost 10% of cats with *S. aureus*.[23] If the animal was MRSA-negative, the recommendations would be the same, with a focus on hygiene to reduce the risk of human-pet transmission.

Pet screening could be considered in the context of a broader household approach to recurrent MRSA infections in people, alongside testing or treatment of all human household members,[198] but only if there is a specific plan for the pet results (e.g. short-term removal from the household to allow the positive pet to naturally eliminate MRSA while the humans are being treated, and in extreme situations, with re-testing prior to re-entry into the home after people and environmental reservoirs also have been shown to be negative). It is possible that, if owners are diagnosed instead with MRSP, MRSS or another MRS known to be linked to companion animals, that pet screening may be indicated in these rare situations.

Testing of animals that partake in human hospital visitation programs:

While dogs that visit human hospitals are known to have an elevated risk of MRSA carriage,[189] current guidelines for these programs do not recommend MRSA screening.[223,224] Screening for other MR staphylococci is also not recommended. Good hygiene practices during visitation visits, including but not limited to hand washing by participants *before* and *after* the assistance animal visit, is essential.

Screening of animals in households with high-risk humans:

A relatively large percentage of pets reside in households with individuals who are at increased risk of disease because of age (very young or old), immunosuppressive disorders or treatments, or pregnancy.[225] As awareness of zoonotic infections increases, owners or physicians occasionally inquire about MRSA (or less commonly MRSP) screening of pets in households such as these. However, screening in situations like this is difficult to justify for many reasons. One is that MR staphylococci are not the only relevant (or potentially even the most relevant) zoonotic pathogens that might be shed by a healthy animal. Screening for MR staphylococci while ignoring other opportunistic pathogens is illogical. Further, screening only provides point-in-time information, and an animal that is negative could become exposed any time after testing. Testing is also not likely 100% sensitive. As is discussed above, given the absence of evidence that decolonization therapy would be indicated or effective, the main recommendations for an animal colonized with MR staphylococci would be an emphasis on hygiene practices, such as avoiding contact with typical colonization sites and paying close attention to hygiene practices (especially hand hygiene). In a household with high-risk individuals, those same recommendations would be made for animals that were not colonized because of concerns about exposure to a wide range of other pathogens. Therefore, since the outcome of a positive or negative result would essentially be the same, screening provides little to no benefits.

Conclusions:

There are many areas of concern identified within this document for which insufficient evidence is available to draw definitive conclusions about the management and prevention of MRS infection, colonization, and transmission. Therefore, the recommendations made herein are by consensus of the authors, following careful consideration of the current literature. It is the hope of the authors that this review has helped to reveal the gaps in the veterinary profession's collective knowledge base regarding MRS. In doing so, it has been our intention to stimulate collaborative dialogue and encourage investigators to pursue the types of studies that will inform more definitive guidelines and recommendations in the future.

Table 1. Recent epidemiologic studies evaluating prevalence of carriage of *S. aureus, S. pseudintermedius* and *S. schleiferi* in dogs and cats.

Sample Population	Study Design	Number of pets	*S. aureus*		*S. pseudintermedius*		*S. schleiferi*		Reference
			MSSA	MRSA	MSSP	MRSP	MSSS	MRSS	
Veterinary clinical populations									
University vet hospital (USA)	Case-control	48 | 50 cats[a]	27% | 16%	2% | 4%	23% | 23%	0% | 4%	0% | 2%	2% | 0%	Abraham 2007
University vet hospital (USA)	Case-control	59 | 50 dogs[a]	7% | 12%	2% | 0%	81% | 64%	7% | 2%	17% | 2%	3% | 2%	Griffeth 2008
University vet hospital (Canada)	Cross-sectional	193 dogs	-	0.5%	-	2%	-	0.5%	Hanselman 2008
University vet hospital (Canada)	Case-control	173 | 41 dogs[a]	-	6.4% | 0%	-	34% | 0%	-	4% | 0%	Beck 2012
Veterinary practices (Poland)	Cross-sectional	172 dogs	5.8%	0%	41%	0%	0%	0%	Garbacz 2012
Veterinary practice (Germany)	Cross-sectional	1 dog | 9 cats	-	0% | 22%	-	0%	-	0%	Weiß 2013
University vet hospital (Thailand)	Cross-sectional	100 dogs	3%	1%	55%	45%	12%	17%	Chanchaithong 2014
Veterinary practices (USA)	Cross-sectional	276 dogs or cats	4%	0%	1%	0%	0%	0%	Davis JA 2014
Veterinary practices (Korea)	Cross-sectional	30 dogs[e]	67%	0%	-	0%	-	-	Jang 2014
Veterinary practices (UK)	Cross-sectional	724 dogs	6.5%	1%	11%	0%	-	-	Wedley 2014
Veterinary practices (Lithuania)	Cross-sectional	345 dogs[e] | 40 cats	-	0% | 0%	-	1.4% | 7.5%	-	0% | 0%	Ruzauskas 2015
Human exposed pet populations									
Pet-owning households (Canada)	Cross-sectional	132 dogs | 161 cats[b]	14% | 4.3%	1.5% | 0%	42% | 6%	5% | 1%	0.8% | 0%	0% | 0%	Hanselman 2009
Therapy pets visiting long-term care (Canada)	Longitudinal	96 | 98 dogs[a]	-	7% | 2%	-	0% | 1%	-	0% | 0%	Lefebvre 2009
Pets of veterinary dermatologists (USA & Canada)	Cross-sectional	258 dogs | 160 cats[b]	-	0.8% | 3.8%	-	6.2% | 3.1%	-	0.8% | 0%	Morris 2010
Dog show (Germany)	Cross-sectional	108 dogs	1.8%	0%	14%	0%	0.9%	0%	Walther 2012
Healthy pets (Spain)	Cross-sectional	54 dogs | 12 cats[b]	9.3% | 25%	0% | 0%	23.2% | 8.3%	3.7% | 0%	-	-	Gomez-Sanz 2012
Shelter dogs (Spain)	Cross-sectional	98 dogs	24%	0%	16%	8%	1%	0%	Gomez-Sanz 2013
Pets and shelter dogs (USA)	Cross-sectional	123 dogs	-	0%	-	1.6%	-	0%	Mouney 2013
Pets of MRSA-infected owners (USA)	Longitudinal	71 dogs | 63 cats[b]	43% | 14%[c]	6% | 5%	79% | 14%[c]	1% | 0%	1% | 0%[c,d]	0% | 0%[d]	Iverson 2015

[a]Given as Case *n* or % | Control *n* or %; [b]Given as Dog *n* or % | Cat *n* or %
[c]MSSA & MSSP prevalence rates estimated from a subset of 28 animals; some of these data have not previously been published
[d]*S. schleiferi* subspecies coagulans only; [e]Shelter or kennel dogs also tested, results not summarized here
These papers are limited to those studies testing for multiple staphylococcal species, and do not include studies targeting just S. aureus, S. pseudintermedius, or S. schleiferi

Table 2: Second tier antimicrobial drugs not widely approved in many countries that may be considered for systemic treatment of MRS pyoderma in dogs after susceptibility testing.

DOGS	WHO classification
Chloramphenicol	HI
Doxycycline	HI
Minocycline	HI
Tetracycline	HI
Amikacin	CIA
Gentamicin	CIA
Tobramycin	CIA
Netilmicin	CIA
Rifampicin	CIA

HI: Highly important antimicrobial for human medicine[WHO 2011]
CIA: Critically important antimicrobial for human medicine[WHO 2011]

Table 3: Comparisons among common molecular typing methods for discrimination of MRS

Method	Inter-laboratory comparison	Throughput	Discriminatory power	Comment
Pulsed field gel electrophoresis (PFGE)	Moderate/low?	Moderate	Excellent	Common method but limited by inter-laboratory variation. Good for within-lab comparison of isolates or when reference stains are available.
Spa typing	Excellent	High	Variable (Species dependent)	Widely used tool for routine typing of *S aureus*. Less useful for *S. pseudintermedius.*
Multi-locus sequence typing (MLST)	Excellent	Moderate	Moderate	Good for evolutionary studies and broad comparisons. Not available for MRSS.
Dru typing	Excellent	High	Good	Can only be performed on MR staphylococci.
*SCC*mec typing	Moderate	Moderate	Low	Limited discriminative power. Good for broad characterization of types and evolutionary studies. Not useful for outbreak investigation. Can only be performed on MR staphylococci.
Whole genome sequencing	Excellent	Low	Excellent	Ultimate method that will become the standard as costs and analytical challenges decrease. It can be used to perform any other sequence-based method listed in this table.

References

1. Werckenthin C, Cardoso M, Martel JL,et al: Antimicrobial resistance in staphylococci from animals with particular reference to bovine *S. aureus*, porcine *S. hyicus*, and canine *S. intermedius*. *Vet Res* 2001;32:341-
2. Chambers HF. Methicillin resistance in staphylococci: molecular and biochemical basis and clinical implications. *Clin Microbiol Rev* 1997;10:781-
3. Morris DO, Rook KA, Shofer FS, et al: Screening of *Staphylococcus aureus*, *S. intermedius*, and *S. schleiferi* isolates obtained from small companion animals for antimicrobial resistance: A retrospective review of 749 isolates (2003-2004). *Vet Dermatol* 2006;17:332-
4. Jones RD, Kania SA, Rohrbach BW,et al: Prevalence of oxacillin- and multidrug-resistant staphylococci in clinical samples from dogs: 1,772 samples (2001-2005). *J Am Vet Med Assoc* 2007;230:221-
5. Rosenstein R, Gotz F. What distinguishes highly pathogenic staphylococci from medium- and non-pathogenic? *Current Topics Microbiol Immunol* 2013;358:33-89.
6. Strommenger B, Bartels MD, Layer KK, et al. Evolution of methicillin-resistant *Staphylococcus aureus* towards increasing resistance. *J Antimicrob Chemother* 2014;69:616-622.
7. Kadlec K, Schwarz S. Antimicrobial resistance of *Staphylococcus pseudintermedius*. *Vet Dermatol* 2012;23:276-e55.
8. Locke JB, Zuill DE, Scharn CR, et al. Linezolid-resistant *Staphylococcus aureus* strain 1128105, the first known clinical isolate possessing the cfr multidrug resistance gene. *Antimicrob Agents Chemother* 2014;58:6592-6598.
9. Friaes A, Resina C, Manuel V, et al. Epidemiological survey of the first case of vancomycin-resistant *Staphylcococcus aureus* infection in Europe. *Epidemiol Infect* 2015;143:745-748.
10. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol* 2005;26:166-174.
11. Bemis DA, Jones RD, Hiatt LE, et al: Comparison of tests to detect oxacillin resistance in *Staphylococcus intermedius*, *Staphylococcus schleiferi*, and *Staphylococcus aureus* isolates from canine hosts. *J Clin Microbiol* 44:3374, 2006
12. Kawakami T, Shibata S, Murayama N, *et al*. Antimicrobial susceptibility and methicillin resistance in *Staphylococcus pseudintermedius* and *Staphylococcus schleiferi* subsp. *coagulans* isolated from dogs with pyoderma in Japan. *J Vet Med Sci* 2010; 72: 1615-1619.
13. Dryden MS. Skin and soft tissue infection: microbiology and epidemiology. *Int J Antimicrob Agents* 2009;33(suppl 3):2-7.
14. Stevens DL, Bismo AL, Chamber HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections. *Clin Infect Dis* 2005;41:1373-1406.

15. Stevens DL, Bismo AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2014;1-43.
16. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:1-38.
17. Beco L, Guaguere E, Lorente Mendez C, et al. Suggested guidelines for using systemic antimicrobials in bacterial skin infections (2): antimicrobial choice, treatment regimens and compliance. *Vet Record* 2013;172:156-60.
18. Hillier A, Lloyd DH, Weese JS, et al. Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases). *Vet Dermatol* 2014;
19. Boutiba-Ben Boubaker I, Ben Abbes R, Ben Abdallah H, et al. Evaluation of a cefoxitin disk diffusion test for the routine detection of methicillin-resistant *Staphylococcus aureus*. *Clinical Microbiol Infect* 2004;10:762–765.
20. Berger-Bachi B, Rohrer S. Factors influencing methicillin resistance in staphylococci. *Arch Microbiol* 2002;178:165-
21. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012;18:268-81.
22. Detwiler A, Bloom P, Petersen A, et al. Multi-drug and methicillin resistance of staphylococci from canine patients at a veterinary teaching hospital (2006-2011). *Vet Quarterly* 2013;33:60-67..
23. Iverson SA, Brazil AM, Ferguson JM, et al. Anatomical patterns of colonization of pets with staphylococcal species in homes of people with methicillin-resistant *Staphylococcus aureus* (MRSA) skin or soft tissue infection (SSTI). *Vet Microbiol* 2015;176:202-208.
24. Otto M. *Staphylococcus* colonization of the skin and antimicrobial peptides. *Expert Rev Dermatol* 2010;5:183-195.
25. Allaker RP, Jensen L, Lloyd DH, et al. Colonization of neonatal puppies by staphylococci. *British Vet J* 1992;148:523-528.
26. Paul NC, Damborg P, Guardabassi L. Dam-to-offspring transmission and persistence of *Staphylococcus pseudintermedius* clones within dog familes. *Vet Dermatol* 2014;25:3-e2.
27. Paul, NC, Bargman, SC, Moodley, A, et al.., *Staphylococcus pseudintermedius* colonization patterns and strain diversity in healthy dogs: A cross-sectional and longitudinal study. *Vet. Microbiol*. 2012;160, 420-427.
28. Blank
29. Abraham JL, Morris DO, Griffeth GC, et al: Surveillance of healthy cats and cats with inflammatory skin disease for colonization of the skin by methicillin-resistant coagulase-positive staphylococci and *Staphylococcus schleiferi* ssp. *schleiferi*. *Vet Dermatol* 2007;18:252-

30. Griffeth GC, Morris DO, Abraham JL, et al. Screening for skin carriage of methicillin-resistant coagulase-positive staphylococci and Staphylococcus schleiferi in dogs with healthy and inflamed skin. Veterinary Dermatology 2008; 19:142-149.
31. Misic AM, Davis MF, Tyldsley AS, et al. The shared microbiota of humans and companion animals as evaluated from *Staphylococcu*s carriage sites. *Microbiome* 2015;3:2.
32. Morris DO**,** Lautenbach E, Zaoutis T, et al. Potential for pet animals to harbor methicillin-resistant *Staphylococcus aureus* (MRSA) when residing with human MRSA patients. *Zoonoses Pub Health*, 2012; 59:286-93.
33. Davis MF, Iverson SA, Baron P, et al. The role of the household in transmission of meticillin-resistant *Staphylococcus aureus* and other staphylococci. *Lancet Infect Dis* 2012;12:703-716*.*
34. Nouwen JL, Ott A, Kluytmans-Vandenbergh MF, et al. Predicting the *Staphylococcus aureus* nasal carrier state: derivation and validation of a "culture rule". *Clin Infect Dis* 2004;15:806-811.
35. Saijonmaa-Koulumies LE, Lloyd DH. Colonization of the canine skin with bacteria. *Vet Dermatol* 1996;7:153-162.
36. Aldeyab MA, Monnet DL, Lopez-Lozano JM, et al. Modelling the impact of antibiotic use and infection control practices on the incidence of hospital-acquired methicillin-resistant *Staphylococcus aureus*: a time-series analysis. *J Antimicrob Chemother* 2008;62:593-600.
37. Beck KM, Waisglass SE, Dick HNL, et al. Prevalence of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) from skin and carriage sites of dogs after treatment of their methicillin-resistant or methicillin-sensitive staphylococcal pyoderma. *Vet Dermatol* 2012;23:369-375.
38. Faires MC, Traverse M, Tater KC, et al. Methicillin-resistant and susceptible *Staphylococcus aureus* infections in dogs. *Emerg Infect Dis* 2010;16:69-75.
39. Cain CL, Morris DO, Rankin SC. Epidemiologic characterization of *Staphylococcus schleiferi* infections in dogs and identification of clinical risk factors for oxacillin resistance. *J Am Vet Med Assoc* 2011;239:1566–1573.
40. Bannoehr J, Guardabassi L. *Staphylcoccus pseudintermedius* in the dog: taxonomy, diagnostics, ecology, epidemiology and pathogenicity. *Vet Dermatol* 2012;23:253-e52.
41. Pinchbech LR, Cole LK, Hillier A, et al. Pulsed-field gel electrophoresis patterns and antimicrobial susceptibility phenotypes for coagulase-positive staphylococcal isolates from pustules and carriage sites in dogs with superficial bacterial folliculitis. *Am J Vet Res* 2007;68:535-42.
42. Laabei M, Recker M, Rudkin JK, et al. Predicting the virulence of MRSA from its genome sequence. *Genome Res* 2014;24:839-849.
43. Cheng AG, McAdow M, Kim HK, et al. Contribution of coagulases toward *Staphylococcus aureus* disease and protective immunity. *PLoS Path* 2010;6:e1001036.
44. Guggenberger C, Wolz L, Morrissey JA, et al. Two distinct coagulase-dependent barriers protect *S. aureus* from neutrophils in a three-dimensional in vitro infection model. *PLoS Path* 2012;8:e1002434.

45. Hajek V. *Staphylococcus intermedius*, a new species isolated from animals. *Int J Syst Bacteriol* 1976;26:401-408.
46. Berg JN, Wendell DE, Vogelweid C, et al. Identification of the major coagulase positive *Staphylococcus* sp. of dogs as *Staphylococcus intermedius*. *Am J Vet Res* 1984; 45:1307-9.
47. Bannoehr J, Ben Zakour NL, Waller AS, et al: Population genetic structure of the *Staphylococcus intermedius* group: Insights into *agr* diversification and emergence of methicillin-resistant strains. *J Bacteriol* 189:8685,2007
48. Sasaki T, Kikuchi K, Tanaka Y, et al : Reclassification of phenotypically identified *Staphylococcus intermedius* strains. *J Clin Microbiol* 45:2770,2007
49. Fitzgerald JR. The *Staphylococcus intermedius* group of bacterial pathogens: species re-classificiation, pathogenesis and the emergence of meticillin resistance. *Vet Dermatol* 2009;20:490-495.
50. Bardiau M, Yamakazi K, Ote I, et al. Characterization of methicillin-resistant *Staphylococcus pseudintermedius* isolated from dogs and cats. *Microbiol Immunol* 2013;57:496-501.
51. Hartmann FA,,White DG, West SEH, et al. Molecular characterization of *Staphylococcus intermedius* carriage by healthy dogs and comparison of antimicrobial susceptibility patterns to isolates from dogs with pyoderma. *Vet Microbiol* 2005; 108:119-131.
52. Harvey RG, Noble WC. Aspects of nasal, oropharyngeal and anal carriage Of Staphylococcus intermedius in normal dogs and dogs with pyoderma. Vet. Dermatol. 1998;9:99-104.
53. Rubin, JE, Chirino-Trejo M Prevalence, sites of colonization, and antimicrobial resistance among *Staphylococcus pseudintermedius* isolated from healthy dogs in Saskatoon, Canada. J Vet Diag Invest 2011;23:351-354.
54. Lilenbaum W, Nunes ELC, Azeredo MAI. Prevalence and antimicrobial susceptibility of staphylococci isolated from the skin surface of clinically normal cats. *Lett Appl Microbiol* 1998;27:224-
55. Lilenbaum W, Esteves AL, Souza GN. Prevalence and antimicrobial susceptibility of staphylococci isolated from saliva of clinically normal cats. *Lett in Appl Microbiol 1999;*28:448-
56. Patel A, Lloyd DH, Lamport AI. Antimicrobial resistance of feline staphylococci in south-eastern England. *Vet Dermatol* 1999;10:257-
57. Igimi S, Atobe H, Tohya Y, et al: Characterization of the most frequently encountered *Staphylococcus* sp. in cats. Vet Microbiol 1994;39: 255-
58. Frank LA, Kania SA, Hnilica KA, et al: Isolation of *Staphylococcus schleiferi* from dogs with pyoderma. *J Am Vet Med Assoc* 2003;222:451-
59. May ER, Hnilica KA, Frank LA, et al: Isolation of *Staphylococcus schleiferi* from healthy dogs and dogs with otitis, pyoderma, or both. *J Am Vet Med Assoc* 2005;227:928-
60. Hernández JL, Calvo J, Sota R et al: Clinical and microbiological characteristics of 28 patients with *Staphylococcus schleiferi* infection. *Eur J Clin Microbiol Infect Dis* 2001;20:153-

61. Rook KA, Brown DC, Rankin SC, et al. Case-control study of *Staphylococcus lugdunensis* infection isolates from small companion animals. Vet Dermatol 2012;23:476-480.
62. Cain CL, Morris DO, O'Shea K, et al. Genotypic relatedness and phenotypic characterization of *Staphylococcus schleiferi* subspecies from canine clinical isolates. *Am J Vet Res* 2011;72:96-102.
63. Misic AM, Cain CL, Morris DO, et al. Complete genome sequence and methylome of *Staphylococcus schleiferi*, an important cause of skin and ear infections in veterinary medicine. *Genome Announce* 2015;3:e01011-15.
64. Kern A, Perreten V. Clinical and molecular features of methicillin-resistant, coagulase-negative staphylococci of pets and horses. *J Antimicrob Chemother* 2013;68:1256-66.
65. Ziebuhr W, Hennig S, Eckart M, et al. Nosocomial infections by *Staphylococcus epidermidis*: how a commensal bacterium turns into a pathogen. *Int J Antimicrob Agents* 2006; 28(suppl 1):s14-20.
66. Garcia-Vazquez E, Fernandez-Rufete A, Hernandez-Torres A, et al. When is coagulase-negative bacteraemia clinically significant? *Scand J Infect Dis* 2013;45:664-71.
67. Rogers KL, Fey PD, Rupp ME. Coagulase-negative staphylococcal infections. *Infect Dis Clin North Amer* 2009;23:73-98.
68. Piette A, Verschraegen G. Role of coagulase-negative staphylococci in human disease. *Vet Microbiol* 2009; 134:45-54.
69. Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. *Clin Microbiol Rev* 2014; 27:870-926
70. Bagcigil FA, Moodley A, Baptiste, KE, et al. Occurrence, species distribution, antimicrobial resistance and clonality of methicillin- and erythromycin-resistant staphylococci in the nasal cavity of domestic animals. *Vet Microbiol* 2007;15:307-315.
71. Baragundi MC, Solabannavar SS, Gokale SK, et al. Methicillin and multidrug resistant coagulase negative staphylococci nasal carriage in medical students. *J Communic Dis* 2012;44:231-7.
72. Diederen BMW, Kluytmans JAJAW: The emergence of infections with community-associated methicillin resistant *Staphylococcus aureus*. *J Infect* 2006;52:157-
73. King MD, Humphrey BJ, Wang YF, et al: Emergence of community-acquired methicillin-resistant *Staphylococcus aureus* USA 300 clone as the predominant cause of skin and soft-tissue infections. *Ann Intern Med* 2006;144:309-
74. Fey PD, Said-Salim B, Rupp ME, et al: Comparative molecular analysis of community- or hospital-acquired methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother* 2003 ;47:196-
75. Graham PL, Lin SX, Larson EL. A U.S. population-based survey of *Staphylococcus aureus* colonization. Ann Intern Med 2006;144:318-
76. Del Giudice P, Blanc V, Durupt F, et al : Emergence of two populations of methicillin-resistant *Staphylococcus aureus* with distinct epidemiological, clinical, and biological features, isolated from patients with community-acquired skin infections. *Br J Dermatol* 2006;154:118-

77. Lin Y, Barker E, Kislow J, et al. Evidence of multiple virulence subtypes in nosocomial and community-associated MRSA genotypes in companion animals from the upper midwestern and northeastern United States. *Clin Med Res* 2011;9:7-16.
78. Weese JS, Dick H, Willey BM, et al. Suspected transmission of methicillin-resistant *Staphylococcus aureus* between domestic pets and humans in veterinary clinics and in the household. *Vet. Microbiol* 2006;115:148-55.
79. McCarthy AJ, Lindsay JA, Loeffler A. Are all methicillin-resistant *Staphylococcus aureus* (MRSA) equal in all hosts? Epidemiological and genetic comparison between animal and human MRSA. *Vet Dermatol* 2012;23:267-75.
80. Bryan J, Frank LA, Rohrbach BW, et al. Treatment outcome of dogs with meticillin-resistant and meticillin-susceptible *Staphylococcus pseudintermedius* pyoderma. *Vet Dermatol* 2012;23:361-368.
81. Perreten V, Kadlec K, Schwarz S, et al. Clonal spread of methicillin-resistant *Staphylococcus pseudintermedius* in Europe and North America: an international multicenter study. *J Antimicrob Chemother* 2010;65:1145-54.
82. Cain CL. Antimicrobial resistance in staphylococci in small animals. *Vet Clin North Amer Sm Anim Pract* 2013;43:19-40
83. Kania SA, Williamson NL, Frank LA, *et al.* Methicillin resistance of staphylococci isolated from the skin of dogs with pyoderma. *Am J Vet Res* 2004; 65: 1265-1268.
84. Kunder DA, Cain CL, O'Shea K, et al. Genotypic relatedness and antimicrobial resistance of Staphylococcus schleiferi in clinical samples from dogs in different geographic regions of the United States. Vet Dermatol 2015;26:406-e94.
85. Sasaki T, Tsubakishita S, Tanaka Y, et al. Multiplex-PCR method for species identification of coagulase-positive staphylococci. *J Clin Microbiol* 2010;48:765-769.
86. Silva MB, Ferreira FA, Garcia LN, et al. An evaluation of matrix-assisted laser desorption ionization time-of-flight mass spectrometry for the identification of *Staphylococcus pseudintermedius* isolates from canine infections. *J Vet Diagn Invest* 2015;27:231-235.
87. Decristophoris P, Fasola A, Benagli C, et al. Identification of *Staphylococcus intermedius* Group by MALDI-TOF MS. *Syst Appl Microbiol* 2011;34::45-51.
88. Murugaiyan J, Walther B, Stamm I, et al. Species differentiation within the Staphylococcus intermedius group using a refined MALDI-TOF MS database. *Clin Microbiol Infect* 2014;;20:1007-1015.
89. Lee JH, Jeong JM, Park YH, et al. Evaluation of the methicillin-resistant *Staphylococcus aureus* (MRSA)-Screen latex agglutination test for detection of MRSA of animal origin. J Clin Microbiol 2004;42:2780-2782.
90. CLSI CLSI VET01-A4,
91. http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_6.0_Breakpoint_table.pdf Accessed April 27, 2016
92. Schissler JR, Hillier A, Daniels JB, et al. Evaluation of Clinical Laboratory Standards Institute interpretive criteria for methicillin-resistant *Staphylococcus pseudintermedius* isolated from dogs. *J Vet Diagn Invest* 2009;21:684-688.

93. Wu MT, Burnham CA, Westblade LF, et al. Evaluation of oxacillin and cefoxitin disk and MIC breakpoints for prediction of methicillin resistance in human and veterinary isolates of *Staphylococcus intermedius* Group. *J Clin Microbiol* 2016;54:535-542.
94. Bemis DA, Jones RD, Videla R, et al. Evaluation of cefoxitin disk diffusion breakpoint for detection of methicillin resistance in *Staphylococcus pseudintermedius* isolates from dogs. *J Vet Diagn Invest* 2012;24:964-967.
95. Mueller RS, Bergvall K, Bensignor E *et al*. A review of topical therapy for skin infections with bacteria and yeast. *Vet Dermatol* 2012; 23: 330-341.
96. Loeffler A, Baines SJ, Toleman MS *et al. In vitro* activity of fusidic acid and mupirocin against coagulase-positive staphylococci from pets. *J Antimicrob Chemother* 2008;62:1301-1304.
97. Boyen F, Verstappen KM, De Bock M *et al. In vitro* antimicrobial activity of miconazole and polymyxin B against canine meticillin-resistant *Staphylococcus aureus* and meticillin-resistant *Staphylococcus pseudintermedius* isolates. *Vet Dermatol* 2012;23:381-385.
98. Clark SM, Loeffler A, Bond R. Susceptibility *in vitro* of canine methicillin-resistant and -susceptible staphylococcal isolates to fusidic acid, chlorhexidine and miconazole: opportunities for topical therapy of canine superficial pyoderma. *J Antimicrob Chemother* 2015;70:2048-2052.
99. Murayama N, Nagata M, Terada Y *et al. In vitro* antiseptic susceptibilities for *Staphylococcus pseudintermedius* isolated from canine superficial pyoderma in Japan. *Vet Dermatol* 2013; 24: 126-129.
100. Valentine BK, Dew W, Yu A *et al*. *In vitro* evaluation of topical biocide and antimicrobial susceptibility of *Staphylococcus pseudintermedius* from dogs*. Vet Dermatol* 2012; 23: 493-495.
101. Loeffler A, Cobb MA, Bond R. Comparison of a chlorhexidine and a benzoyl peroxide shampoo as sole treatment in canine superficial pyoderma. *Vet Rec* 2011; 169: 249.
102. Murayama N, Nagata M, Terada Y *et al*. Efficacy of a surgical scrub including 2% chlorhexidine acetate for canine superficial pyoderma. *Vet Dermatol* 2010; 21: 586-592.
103. Borio S, Colombo S, La Rosa G *et al*. Effectiveness of a combined (4% chlorhexidine digluconate shampoo and solution) protocol in MRS and non-MRS canine superficial pyoderma: a randomized, blinded, antibiotic-controlled study. *Vet Dermatol* 2015; 26: 339-344.
104. Manian FA. Asymptomatic nasal carriage of mupirocin-resistant, methicillin-resistant *Staphylococcus aureus* (MRSA) in a pet dog associated with MRSA infection in household contacts. *Clin Infect Dis* 2003; 36: e26-28.
105. Liu Q, Zhao H, Han L, Shu W, Wu Q, Ni Y. Frequency of biocide-resistant genes and susceptibility to chlorhexidine in high-level mupirocin-resistant, methicillin-resistant Staphylococcus aureus (MuH MRSA). *Diagn Microbiol Infect Dis* 2015;82:278-83.
106. Johnson RC, Schlett CD, Crawford K et al. Recurrent methicillin-resistant *Staphylococcus aureus* cutaneous abscesses and selection of reduced chlorhexidine susceptibility during chlorhexidine use. *J Clin Microbiol* 2015; 53:

3677-3682.
107. Yu F, Liu Y, Lu C *et al*. Dissemination of fusidic acid resistance among *Staphylococcus aureus* clinical isolates. *BMC Microbiol* 2015; 15: 210.
108. McConeghy KW, Mikolich DJ, LaPlante KL. Agents for the decolonization of methicillin-resistant *Staphylococcus aureus. Pharmacotherapy* 2009; 29: 263-280.
109. BNF
110. Heng YK, Tan KT, Sen P *et al*. *Staphylococcus aureus* and topical fusidic acid use: results of a clinical audit on antimicrobial resistance. *Int J Dermatol* 2013; 52: 876-881.
111. Poovelikunnel T, Gethin G, Humphreys H. Mupirocin resistance: clinical implications and potential alternatives for the eradication of MRSA. *J Antimicrob Chemother* 2015; 70: 2681-2692.
112. Lloyd DH. Alternatives to conventional antimicrobial drugs: a review of future prospects. *Vet Dermatol* 2012; 23: 299-304.
113. Pariser M, Gard S, Gram L *et al*. An *in vitro* study to determine the minimal bactericidal concentration of sodium hypochlorite (bleach) required to inhibit meticillin-resistant *Staphylococcus pseudintermedius* strains isolated from canine skin. *Vet Dermatol* 2013; 24: 632-634.
114. Banovic F, Lemo N. *In vitro* evaluation of the use of diluted sodium hypochlorite (bleach) against *Staphylococcus pseudintermedius, Pseudomonas aeruginosa* and *Malassezia pachydermatis. Vet Dermatol* 2014; 25: 233-234.
115. Beco L, Guaguère E, Lorente Méndez C *et al*. Suggested guidelines for using systemic antimicrobials in bacterial skin infections (1): diagnosis based on clinical presentation, cytology and culture. *Vet Rec* 2013; 172: 72-78.
116. Summers JF, Brodbelt DC, Forsythe PJ et al. The effectiveness of systemic antimicrobial treatment in canine superficial and deep pyoderma: a systematic review. *Vet Dermatol* 2012; 23: 305-329.
117. Tomlin J, Pead MJ, Lloyd DH *et al*. Methicillin-resistant *Staphylococcus aureus* infections in 11 dogs. *Vet Rec* 1999; 144: 60-64.
118. Loeffler A, Linek M, Moodley A *et al*. First report of multiresistant, *mecA*-positive *Staphylococcus intermedius* in Europe: 12 cases from a veterinary dermatology referral clinic in Germany. *Vet Dermatol* 2007; 18: 412-421.
119. McCarthy AJ, Harrison EM, Stanczak-Mrozek K *et al*. Genomic insights into the rapid emergence and evolution of MDR in *Staphylococcus pseudintermedius*. *J Antimicrob Chemother* 2015; 70: 997-1007.
120. Gurusamy KS, Koti R, Toon CD *et al*. Antibiotic therapy for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) in non-surgical wounds. *Cochrane Database Syst Rev* 2013; 11:CD010427.
121. Casagrande Proietti P, Bietta A, Coletti M *et al*. Insertion sequence IS256 in canine pyoderma isolates of *Staphylococcus pseudintermedius* associated with antibiotic resistance. *Vet Microbiol* 2012; 157: 376-382.
122. Liu YC, Huang WK, Cheng DL. Antibacterial activity of cefpodoxime *in vitro*. *Chemotherapy* 1997; 43: 21-26.

123. Chanchaithong P, Prapasarakul N. Occurrence and characterization of inducible clindamycin resistance in canine methicillin-resistant *Staphylococcus pseudintermedius. Vet J* 2015. pii: S1090-0233(15)00342-1.
124. Lewis II J, Jorgensen JH. Inducible clindamycin resistance in staphylococci: Should clinicians and microbiologists be concerned? *Clin Infect Dis* 40: 280-285.
125. Maaland MG, Papich MG, Turnridge J, et al. Pharmacodynamics of doxycycline and tetracycline against *Staphylococcus pseudintermedius*: Proposal of canine-specific breakpoints for doxycycline. *J Clin Microbiol* 2013; 51: 3547–3554.
126. Hnot ML, Cole LK, Lorch G et al. Evaluation of canine-specific minocycline and doxycycline susceptibility breakpoints for meticillin-resistant *Staphylococcus pseudintermedius* isolates from dogs. *Vet Dermatol*; 26: 334-338.
127. Füzi M. Has the use of fluoroquinolones facilitated the widespread dissemination of methicillin-resistant *Staphylococcus aureus* and extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* in the healthcare setting? *Acta Microbiol Immunol Hung* 2014; 61: 399-405.
128. Frank LA, Loeffler A. Meticillin-resistant *Staphylococcus pseudintermedius*: clinical challenge and treatment options. *Vet Dermatol* 2012; 23: 283-291.
129. Papich MG. Selection of antibiotics for meticillin-resistant *Staphylococcus pseudintermedius*: time to revisit some old drugs? *Vet Dermatol* 2012; 23: 352-360.
130. WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). Crticially Important Antimicrobials for Human Meidicine. 3rd Revision 2011. http://www.who.int/foodsafety/publications/antimicrobials-third/en/. Accessed 27th February 2016
131. Weese JS. Issues regarding the use of vancomycin in companion animals. *J Am Vet Med Assoc* 2008; 233: 565-567.
132. Nilsson O. Vancomycin resistant enterococci in farm animals - occurrence and importance. *Infect Ecol Epidemiol* 2012; 2.
133. O'Driscoll T, Crank CW. Vancomycin-resistant enterococcal infections: epidemiology, clinical manifestations, and optimal management. *Infect Drug Resist* 2015; 8: 217-230.
134. Zhang S, Sun X, Chang W et al. Systematic review and meta-analysis of the epidemiology of vancomycin-intermediate and heterogeneous vancomycin-intermediate *Staphylococcus aureus* isolates. *PLoS One* 2015; 19; 10: e0136082.
135. Morris DO, Mauldin EA, O'shea K, et al: Clinical, microbiological, and molecular characterization of methicillin-resistant *Staphylococcus aureus* infections of cats. Am J Vet Res 2006;67:1421-
136. Yilmaz M, Elaldi N, Balkan İİ *et al*. Mortality predictors of *Staphylococcus aureus* bacteremia: a prospective multicenter study. *Ann Clin Microbiol Antimicrob* 2016; 15: 7.
137. Tomlin repeat
138. Microarray study from Anette

139. Youn JH, Koo HC, Ahn KJ *et al*. Determination of staphylococcal exotoxins, SCC*mec* types, and genetic relatedness of *Staphylococcus intermedius* group isolates from veterinary staff, companion animals, and hospital environments in Korea. *J Vet Sci* 2011; 12: 221-226.
140. Soedarmanto I, Kanbar T, Ülbegi-Mohyla H *et al*. Genetic relatedness of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) isolated from a dog and the dog owner. *Res Vet Sci* 2011; 91: e25-27.
141. Iyori K, Futagawa-Saito K, Hisatsune J *et al*. *Staphylococcus pseudintermedius* exfoliative toxin EXI selectively digests canine desmoglein 1 and causes subcorneal clefts in canine epidermis. *Vet Dermatol* 2011; 22: 319-326.
142. Chen CJ, Wang SC, Chang HY *et al*. Longitudinal analysis of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* carriage in healthy adolescents. *J Clin Microbiol* 2013; 51: 2508-2514.
143. Kock R, Becker K, Cookson B *et al*. Systematic literature analysis and review of targeted preventive measures to limit healthcare-associated infections by meticillin-resistant *Staphylococcus aureus*. *Euro Surveill* 2014; 19: 29.
144. Loeb MB, Main C, Eady A *et al*. Antimicrobial drugs for treating methicillin-resistant *Staphylococcus aureus* colonization. *Cochrane Database Syst Rev* 2003; 4: CD003340.
145. Wertheim HF, Vos MC, Ott A *et al*. Risk and outcome of nosocomial *Staphylococcus aureus* bacteraemia in nasal carriers versus non-carriers. *Lancet* 2004; 364: 703-705.
146. Gupta K, Strymish J, Abi-Haidar Y *et al*. Preoperative nasal methicillin-resistant *Staphylococcus aureus* status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. *Infect Control Hosp Epidemiol* 2011; 32:791-796.
147. Harbarth S, Huttner B, Gervaz P *et al*. Risk factors for methicillin-resistant *Staphylococcus aureus* surgical site infection. *Infect Control Hosp Epidemiol* 2008; 29: 890-893.
148. Pinchbeck LR, Cole LK, Hillier A *et al*. Genotypic relatedness of staphylococcal strains isolated from pustules and carriage sites in dogs with superficial bacterial folliculitis. *Am J Vet Res* 2006; 67: 1337-1346.
149. Nazarali A, Singh A, Moens NM *et al*. Association between methicillin-resistant *Staphylococcus pseudintermedius* carriage and the development of surgical site infections following tibial plateau leveling osteotomy in dogs. *J Am Vet Med Assoc* 2015; 247: 909-916.
150. Windahl U, Reimegård E, Holst BS *et al*. Carriage of methicillin-resistant *Staphylococcus pseudintermedius* in dogs-a longitudinal study. *BMC Vet Res* 2012; 8: 34.
151. Lefebvre SL, Reid-Smith RJ, Waltner-Toews D *et al*. Incidence of acquisition of methicillin-resistant *Staphylococcus aureus, Clostridium difficile*, and other health-care-associated pathogens by dogs that participate in animal-assisted interventions. *J Am Vet Med Assoc* 2009; 234: 1404-1417.
152. Simou C, Hill PB, Forsythe PJ *et al*. Species specificity in the adherence of staphylococci to canine and human corneocytes: a preliminary study. *Vet*

Dermatol 2005; 16: 156-161.
153. Wagenvoort JH, Sluijsmans W, Penders RJ. Better environmental survival of outbreak vs. sporadic MRSA isolates. *J Hosp Infect* 2000; 45: 231-234.
154. Smith SM, Eng RH, Padberg FT. Survival of nosocomial pathogenic bacteria at ambient temperature. *J Med* 1996; 27: 293-302.
155. Scott GM, Thomson R, Malone-Lee J *et al*. Cross-infection between animals and man: possible feline transmission of *Staphylococcus aureus* infection in humans? *J Hosp Infect* 1988; 12: 29-34.
156. Soares-Magalhães RJ, Loeffler A, Lindsay J *et al*. Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) infection in dogs and cats: a case-control study. Vet Res 2010;41:55-
157. Laarhoven LM, de Heus P, van Luijn J *et al*. Longitudinal study on methicillin-resistant *Staphylococcus pseudintermedius* in households. *PLoS One* 2011; 6: e27788.
158. van Duijkeren E, Kamphuis M, van der Mije IC *et al*. Transmission of methicillin-resistant *Staphylococcus pseudintermedius* between infected dogs and cats and contact pets, humans and the environment in households and veterinary clinics. *Vet Microbiol* 2011; 150: 338-343.
159. Lee CR, Lee JH, Park KS *et al*. Quantitative proteomic view associated with resistance to clinically important antibiotics in Gram-positive bacteria: a systematic review. *Front Microbiol* 2015; 6: 828-
160. Nielsen KL, Pedersen TM, Udekwu KI et al. Fitness cost: a bacteriological explanation for the demise of the first international methicillin-resistant *Staphylococcus aureus* epidemic. *J Antimicrob Chemother* 2012; 67: 1325-1332.
161. Noto MJ, Fox PM, Archer GL. Spontaneous deletion of the methicillin resistance determinant, *mecA*, partially compensates for the fitness cost associated with high-level vancomycin resistance in *Staphylococcus aureus. Antimicrob Agents Chemother* 2008; 52: 1221-1229.
162. Ender M, McCallum N, Adhikari R, Berger-Bächi B. Fitness cost of SCC*mec* and methicillin resistance levels in *Staphylococcus aureus*. *Antimicrob Agents Chemother* 2004; 48: 2295-2297.
163. Cookson B, Peters B, Webster M *et al*. Staff carriage of epidemic methicillin-resistant *Staphylococcus aureus. J Clin Microbiol* 1989; 27: 1471-1476.
164. Loeffler A, Pfeiffer DU, Lindsay JA *et al*. Lack of transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) between apparently healthy dogs in a rescue kennel. *Vet Microbiol* 2010; 141: 178-181.
165. Saijonmaa-Koulumies L, Parsons E, Lloyd DH. Elimination of *Staphylococcus intermedius* in healthy dogs by topical treatment with fusidic acid. *J Small Anim Pract* 1998; 39: 341-347.
166. Kadlec K, Schwarz S, Goering RV and Weese JS. Direct repeat unit (dru) typing of methicillin-resistant Staphylococcus pseudintermedius from dogs and cats. *Journal of Clinical Microbiology*. 2015.
167. 2. Grönthal T, Moodley A, Nykäsenoja S, et al. Large outbreak caused by methicillin resistant *Staphylococcus pseudintermedius* ST71 in a Finnish

Veterinary Teaching Hospital--from outbreak control to outbreak prevention. *PLoS ONE*. 2014; 9: e110084.
168. Harris SR, Cartwright EJP, Török ME, et al. Whole-genome sequencing for analysis of an outbreak of meticillin-resistant Staphylococcus aureus: a descriptive study. *The Lancet infectious diseases*. 2013; 13: 130-6.
169. Köser CU, Holden MTG, Ellington MJ, et al. Rapid whole-genome sequencing for investigation of a neonatal MRSA outbreak. *New Engl J Med*. 2012; 366: 2267-75.
170. Koreen L, Ramaswamy SV, Graviss EA, Naidich S, Musser JM and Kreiswirth BN. spa typing method for discriminating among Staphylococcus aureus isolates: implications for use of a single marker to detect genetic micro- and macrovariation. *J Clin Microbiol*. 2004; 42: 792-9.
171. Davis MF, Misic AM, Morris DO, Moss JT, Tolomeo P, Beiting D, Nachamkin I, Lautenbach E; Rankin SC. Genome sequencing reveals strain dynamics of methicillin-resistant *Staphylococcus aureus* in the same household in the context of clinical disease in a person and a dog. *Vet Microbiol* 2015;180:304-7.
172. Perreten V, Kadlec K, Schwarz S, et al. Clonal spread of methicillin-resistant *Staphylococcus pseudintermedius* in Europe and North America: an international multicentre study. *J Antimicrob Chemother*. 2010; 65: 1145-54.
173. Paterson GK, Harrison EM, Murray GG, et al. Capturing the cloud of diversity reveals complexity and heterogeneity of MRSA carriage, infection and transmission. *Nat Commun* 2015;6:6560.
174. Anderson MEC, Montgomery J, Weese JS et al. Infection prevention and control best practices for small animal veterinary clinics. Guelph, Ontario: Canadian Committee on Antibiotic Resistance, 2008.
175. British Small Animal Veterinary A. BSAVA practice guidelines - reducing the risk from MRSA and MRSP. 2011.
176. National Association of State Public Health V. Compendium of Veterinary Standard Precautions. 2006.
177. Jason Stull & Scott Weese (2014). Infection Control in Veterinary Small Animal Practice. *Veterinary Clinics of NA: Small Animal Practice*, 1–2.
178. Nordstrom JM, Reynolds KA, Gerba CP. Comparison of bacteria on new, disposable, laundered, and unlaundered hospital scrubs. *Am J Infect Control* 2012;40:539-543.
179. Pepper T, Hicks G, Glass S, et al. Bacterial contamination of fabric and metal-bead identity card lanyards: A cross-sectional study. *J Infection Pub Health* 2014;7:542-546.
180. López-Alcalde J, Mateos-Mazón M, Guevara M, et al. Gloves, gowns and masks for reducing the transmission of meticillin-resistant *Staphylococcus aureus* (MRSA) in the hospital setting. Cochrane Database Syst Rev. 2015;7:CD007087.
181. Anderson MEC, Sargeant JM, Weese JS. Video observation of hand hygiene practices during routine companion animal appointments and the effect of a poster intervention on hand hygiene compliance. *BMC Veterinary Research* 2014; 10: 106.
182. Huang C, Ma W, Stack S. (2012). The hygienic efficacy of different hand-

drying methods: A review of the evidence. *Mayo Clinic Proceedings* 2012;87: 791–798.
183. Sroka S, Gastmeier P, Meyer E. Impact of alcohol hand-rub use on meticillin-resistant *Staphylococcus aureus*: an analysis of the literature. *J Hosp Infect* 2010;74:204–211.
184. Dettenkofer, M, Spencer RC. Importance of environmental decontamination--a critical view. *JHosp Infect*2007; *65 (Suppl 2):* 55–57.
185. Weese JS, DaCosta T, Button L, et al. Isolation of methicillin-resistant Staphylococcus aureus from the environment in a veterinary teaching hospital. *J Vet Intern Med* 2004:18:468–470.
186. Couto N, Belas A, Kadlec K, et al. Clonal diversity, virulence patterns and antimicrobial and biocide susceptibility among human, animal and environmental MRSA in Portugal. *J Antimicrob Chemother* 2015;70:2483-2487
187. Burgess BA,Morley PS. Veterinary hospital surveillance systems. *Vet Clin North Am Small Anim Pract*. 2014; doi: 10.1111/evj.12234.
188. Loeffler A, Pfeiffer D, Lindsay J et al. Lack of transmission of methicillin-resistant Staphylococcus aureus (MRSA) between apparently healthy dogs in a rescue kennel. *Vet Microbiol*. 2010; 141: 178-81. (repeat)
189. Lefebvre SL, Reid-Smith RJ, Waltner-Toews D, et al. Incidence of acquisition of methicillin-resistant *Staphylococcus aureus, Clostridium difficile*, and other health-care-associated pathogens by dogs that participate in animal-assisted interventions. *J Am Vet Med Assoc*. 2009; 234: 1404-17.
190. Weese JS, Faires M, Rousseau J, et al. Cluster of methicillin-resistant *Staphylococcus aureus* colonization in a small animal intensive care unit. *J Am Vet Med Assoc*. 2007; 231: 1361-4.
191. van Duijkeren E, Kamphuis M, van der Mije IC, et al. Transmission of methicillin-resistant *Staphylococcus pseudintermedius* between infected dogs and cats and contact pets, humans and the environment in households and veterinary clinics. *Vet Microbiol*. 2011; 150: 338-43.
192. Laarhoven LM, de Heus P, van Luijn J. et al. Longitudinal Study on Methicillin-Resistant *Staphylococcus pseudintermedius* in households. *PLoS ONE*. 2011; 6: e27788.
193. Lehner G, Linek M, Bond R, et al. Case-control risk factor study of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) infection in dogs and cats in Germany. *Vet Microbiol*. 2014; 168: 154-60.
194. Nienhoff U, Kadlec K, Chaberny IF, et al. Methicillin-resistant *Staphylococcus pseudintermedius* among dogs admitted to a small animal hospital. *Vet Microbiol*. 2011; 150-.
195. Heller J, Innocent GT, Denwood M, et al. Assessing the probability of acquisition of meticillin-resistant *Staphylococcus aureus* (MRSA) in a dog using a nested stochastic simulation model and logistic regression sensitivity analysis. *Prev Vet Med* 2011; 99: 211-24.
196. Loeffler A, Pfeiffer DU, Lindsay JA, et al. Prevalence of and risk factors for MRSA carriage in companion animals: a survey of dogs, cats and horses. *EpidemiolInfect* 2010; : 1-10.

197. Barton. Canadian CA-MRSA Guidelines. *Can J Infect Dis Med Microbiol*. 2006.
198. Gorwitz RJ, Jernigan DB, Powers JH, et al. Strategies for clinical management of MRSA in the community: summary of an experts' meeting convened by the Centers for Disease Control and Prevention. 2006.
199. Hanselman BA, Kruth S A, Rousseau J, et al. Coagulase positive staphylococcal colonization of humans and their household pets. *Canadian Vet J La Revue Vétérinaire Canadienne* 2009; *50*: 954–958.
200. Morris DO**,** Boston RC, O'Shea K, et al. Prevalence of methicillin-resistant staphylococcal carriage by veterinary dermatology practice staff and their respective pets. *Vet Dermatol* 2010; 21:400-07.
201. Harrison EM, Weinert LA, Holden M, et al. A shared population of epidemic methicillin-resistant Staphylococcus aureus 15 circulates in humans and companion animals. *mBio* 2014; *5* epub. http://doi.org/10.1128/mBio.00985-13.
202. Cuny C, Friedrich A, Kozytska S, et al. Emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) in different animal species. *Int J Med Microbiol* 2010;300:109-17.
203. Baptiste KE, Williams K, Willams NJ, *et al.* Methicillin-resistant staphylococci in companion animals. *Emerg Infect Dis* 2005;11:1942-1944.
204. Lakdawala N, Pham J, Shah M, et al. Effectiveness of low-temperature domestic laundry on the decontamination of healthcare workers' uniforms. *Infect Control Hosp Epidemiol* 2011;*32*:1103–1108. http://doi.org/10.1086/662183
205. Hardy KJ, Gossain S, Henderson N, et al. Rapid recontamination with MRSA of the environment of an intensive care unit after decontamination with hydrogen peroxide vapour. *J Hosp Infect* 2007; 66**:** 360–68.
206. Burden M, Cervantes L, Weed D, Keniston A, Price CS, Albert RK. Newly cleaned physician uniforms and infrequently washed white coats have similar rates of bacterial contamination after an 8-hour workday: a randomized controlled trial. *J Hosp Med* 2011; 6**:** 177–82.
207. Fritz SA, Hogan PG, Hayek G, et al. Household Versus Individual Approaches to Eradication of Community-Associated Staphylococcus aureus in Children: A Randomized Trial. *Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America*, 2012; 54, 743–751. http://doi.org/10.1093/cid/cir919
208. Cluzet VC, Gerber JS, Nachamkin I et al. CDC Prevention Epicenters Program. A randomized controlled trial of the effect of total household decolonization on termination of colonization with methicillin-resistant *Staphylococcus aureus. In* Program and Abstracts of the ID Week Sci Conf, Abstr 1336, Philadelphia, PA. October 11, 2014.
209. Murphy E, Spencer SJ, Young D, Jones B and Blyth MJG. MRSA colonisation and subsequent risk of infection despite effective eradication in orthopaedic elective surgery. *J Bone Joint Surg Br*. 2011; 93: 548-51.
210. Harbarth S, Huttner B, Gervaz P, et al. Risk factors for methicillin-resistant Staphylococcus aureus surgical site infection. *Infection control and hospital*

epidemiology : the official journal of the Society of Hospital Epidemiologists of America. 2008; 29: 890-3.
211. Shukla S, Nixon M, Acharya M, Korim MT and Pandey R. Incidence of MRSA surgical-site infection in MRSA carriers in an orthopaedic trauma unit. *J Bone Joint Surg Br*. 2009; 91: 225-8.
212. Trautmann M, Stecher J, Hemmer W, Luz K and Panknin HT. Intranasal mupirocin prophylaxis in elective surgery. A review of published studies. *Chemotherapy*. 2008; 54: 9-16.
213. Nazarali A, Singh A, Moens NMM, et al. Association between methicillin-resistant Staphylococcus pseudintermedius carriage and the development of surgical site infections following tibial plateau leveling osteotomy in dogs. *Journal of the American Veterinary Medical Association*. 2015; 247: 909-16.
214. Weese JS, Archambault M, Willey BM, et al. Methicillin-resistant *Staphylococcus aureus* in horses and horse personnel, 2000-2002. *Emerging Infect Dis*. 2005; 11: 430-5.
215. Weese JS, Rousseau J, Traub-Dargatz JL, Willey BM, McGeer AJ and Low DE. Community-associated methicillin-resistant *Staphylococcus aureus* in horses and humans who work with horses. *J Am Vet Med Assoc*. 2005; 226: 580-3.
216. Aklilu E, Zunita Z, Hassan L and Cheng CH. Molecular epidemiology of methicillin-resistant Staphylococcus aureus (MRSA) among veterinary students and personnel at a veterinary hospital in Malaysia. *Veterinary Microbiology*. 2013: 1-7.
217. Anderson MEC, Lefebvre SL and Weese JS. Evaluation of prevalence and risk factors for methicillin-resistant *Staphylococcus aureus* colonization in veterinary personnel attending an international equine veterinary conference. *Vet Microbiol*. 2008; 129: 410-7.
218. Burstiner LC, Faires M and Weese JS. Methicillin-Resistant Staphylococcus aureus Colonization in Personnel Attending a Veterinary Surgery Conference. *Vet Surg*. 2010; 39: 150-7.
219. Hanselman BA, Kruth SA, Rousseau J, et al. Methicillin-resistant *Staphylococcus aureus* colonization in veterinary personnel. *Emerging Infect Dis*. 2006; 12: 1933-8.
220. Loeffler A, Pfeiffer DU, Lloyd DH, Smith H, Soares-Magalhaes R and Lindsay JA. Meticillin-resistant *Staphylococcus aureus* carriage in UK veterinary staff and owners of infected pets: new risk groups. *J Hosp Infect*. 2010; 74.
221. Jordan D, Simon J, Fury S, et al. Carriage of methicillin-resistant *Staphylococcus aureus* by veterinarians in Australia. *Aust Vet J*. 2011; 89: 152-9.
222. Faires MC, Tater KC and Weese JS. An investigation of methicillin-resistant *Staphylococcus aureus* colonization in people and pets in the same household with an infected person or infected pet. *J Am Vet Med Assoc*. 2009; 235: 540-3.
223. Lefebvre SL, Golab GC, Christensen E, et al. Guidelines for animal-assisted interventions in health care facilities. *Am J Infect Control*. 2008; 36: 78-85.

224. Murthy R, Bearman G, Brown S, et al. Animals in Healthcare Facilities: Recommendations to Minimize Potential Risks. *Infection control and hospital epidemiology : the official journal of the Society of Hospital Epidemiologists of America*. 2015: 1-22.
225. Stull JW, Peregrine AS, Sargeant JM and Weese JS. Household knowledge, attitudes and practices related to pet contact and associated zoonoses in Ontario, Canada. *BMC public health*. 2012; 12: 553.